



VOLUME 24

*Boston Number*

NUMBER 5

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THE  
MEDICAL CLINICS  
OF  
NORTH AMERICA

*SEPTEMBER, 1940*

PHILADELPHIA AND LONDON

W. B. SAUNDERS COMPANY

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SQUARE, PHILADELPHIA.

MADE IN U. S. A.



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September, 1940

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## SYMPTOMS OF PATIENTS WITH HEART DISEASE AND THEIR INTERPRETATION

DURING the past quarter of a century, remarkable advances have been made in the diagnosis of heart disease and in the quantitative evaluation of congestive failure of the circulation. This progress has been achieved mainly through systematic investigations made with exact chemical and physical methods. As a result, the value of these methods has been overemphasized; and as a corollary of this, in recent years the importance of rational and skilled interpretation of symptoms has been underestimated by the profession. It is thought by many that a good history and proper evaluation of complaints is less important today than in the past. This is a serious misconception.

Before the advent of modern clinical investigation, symptoms were correlated for the most part with the findings of the physical examination, and they in turn with morphologic changes as observed postmortem. Although bedside studies can throw important light on the clinical significance of symptoms, the fundamental nature of symptoms could not be studied in the past because sufficiently sensitive objective methods were not available. With the discovery of new technic in recent

years has come the first study of the mechanism of many symptoms. Hence, the significance and interpretation of symptoms are on a firmer foundation today than ever before.

The fact that complicated instruments are essential to the fundamental study of a symptom does not mean that the physician in his daily practice necessarily has to use these instruments. We must not confuse the use of laboratory methods as a tool of investigation with their use as routine instruments in the care of the patient. Once investigators have established the significance of a clinical phenomenon, the intelligent use of such conclusions usually suffices in the practice of medicine. Thus, with the aid of the galvanometer it has been established that "pulsus irregularis perpetuus" is associated with fibrillations or "circus movements" of the auricles. As a result, today the clinical diagnosis of auricular fibrillation can be made at the bedside with a high degree of accuracy. Similarly, systematic investigations with complicated chemical and physical methods have established the fact that paroxysmal dyspnea or cardiac asthma is the result of active pulmonary engorgement depending on a combination of certain types of cardiac and pulmonary lesions. The results of these studies have made it possible subsequently for the practitioner to use this information at the bedside as an aid to better diagnosis, prognosis and treatment. Hence, clinical investigation has placed the interpretation of symptoms on a more exact basis. The practical gain to the physician from the proper recognition and interpretation of symptoms is greater today than it was some twenty years ago when Sir James Mackenzie emphasized the significance of this problem. Today, therefore, we need to place renewed emphasis and greater attention on the *interpretation* of symptoms.

The story of heart disease is told by the patient, and knowledge of the natural history of the disease and estimation of the degree of circulatory failure depend on the interpretation of this story. Symptoms depend on sensation or a combination of sensations, and the total number of symptoms or complaints is not very great. The symptoms bring the patient to the phys-

ician, and while symptoms are the first signal bell to the patient indicating ill health, they are not invariably early manifestations of disease. Examination with laboratory methods at times reveals advanced structural changes before the appearance of symptoms, as is frequently the case in rheumatic, luetic or hypertensive heart disease. Thus, while intelligent interpretation of symptoms often dispenses with laborious, expensive and painful laboratory tests, we must not rely on symptoms alone.

Since the presence of symptoms depends on the sensitivity of the central nervous system, the same disease may give rise to different degrees of symptoms in different persons. Knowledge and testing of the factors which influence individual variations in symptoms are essential in clinical medicine.

There are relatively few symptoms associated with heart disease and the majority of these originate not in the heart, but in the congested lungs and other organs affected by secondary failure of the heart as a pump. The heart itself is a relatively insensitive organ, and the main sensations attached to it are consciousness of heart action or palpitation, pain or thoracic distress, and nervousness or anxiety. The other common symptoms of heart disease, such as breathlessness (dyspnea), wheezing, fatigue, cough, anorexia, vomiting, epigastric distress, hiccup, flatulence, diarrhea, insomnia, nightmare, terror, delirium, coldness of the extremities, dizziness, giddiness and syncope, usually depend on changes in organs or systems affected by disturbed action of the heart. Cyanosis, jaundice and edema, although recognized at times by the patient, are signs rather than symptoms.

#### CONSCIOUSNESS OF HEART ACTION AND PALPITATION

Consciousness of heart action is often described by the patient as palpitation or as "pounding," "a sudden flop," "fluttering," "thumping," or "turning over" of the heart. Palpitation is frequently a *normal* phenomenon, and during mental excitement or exposure to heat, or following severe exertion, it is a common physiologic experience. During *adolescence* palpita-

tion is a common complaint. Whether this palpitation is related to changes in the glands of internal secretion or to emotional intensity is not known. Palpitation is one of the symptoms following *menopause*, and here it is dependent on vasomotor instability. Some otherwise normal persons are conscious of their heart action all the time, and this may cause them considerable anguish. Such persons are usually innately high strung and hypersensitive.

*Tobacco*—particularly cigarette smoking—can be responsible for annoying palpitation, even in persons with a normal heart, and the relative sensitivity of various persons in this respect varies considerably. In my experience, the tendency to palpitation caused by smoking is increased during fatigue and after respiratory infections. The sensation may develop at any time of day, but it is prone to appear or is accentuated when retiring in the evening. In some persons it is more likely to occur when smoking in the morning before eating. Palpitation caused by the use of tobacco is often associated with premature ventricular beats.

*Tea, coffee, alcohol*, and certain *drugs* such as epinephrine, benzedrine, digitalis, cocaine and other local anesthetics can also cause annoying palpitations. *Giddiness* is frequently associated with palpitation in instances of sudden drop of the arterial pressure, which may accompany various types of emotional strain or the early stage of syncope. Palpitation is common, also, among persons with *aerophagia* resulting from distention of the stomach on pressure on the left side of the diaphragm.

With an increase in the stroke volume of the heart, or sudden change in the rate or rhythm of the heart, palpitation is experienced under various *pathologic conditions*. In these circumstances the patient becomes conscious of his heart action and experiences a throbbing thoracic sensation. Thus, patients with severe anemia or with hyperthyroidism may complain only of palpitation. Premature ventricular beats, tachycardias, and paroxysmal fibrillation and flutter of the auricle may be associated with it. In Adams-Stokes attacks it may be a prominent complaint. Palpitation is a frequent symptom in patients with

arterial hypertension, even in those with good cardiac reserve, because hypertension is frequently associated with vasomotor fluctuations. An enlarged and dilated heart through physical proximity with the thoracic wall can be associated with a sensation of constant palpitation, and sudden changes in cardiac action or rhythm in these patients are particularly apt to produce distressing palpitation. In the clinical syndrome of neuro-circulatory asthenia palpitation is an important component.

In the underlying physiologic mechanisms of palpitation, increased stroke volume, hypersensitivity of the central nervous system and unaccustomed heart action (abnormal rates and rhythms) are the most important factors. It is of some interest that I have observed patients who complained of heart consciousness and palpitation when normal sinus rhythm was reestablished with quinidine after symptomless auricular fibrillation of long duration. In these instances the regular rhythm was the unaccustomed rhythm, and hence was accompanied by palpitation.

Palpitation or heart consciousness is often associated with *anxiety* and *nervousness*. Frequently, as in the presence of a structurally normal heart, this anxiety simply indicates that the patient is a nervous introspective person who attaches a kind of phobia to the heart. If patients with chronic anxiety neuroses develop palpitation of the heart as the result of arrhythmias or organic heart disease, their nervous difficulties are prone to become accentuated. But in the presence of organic heart disease the associated anxiety may be well justified, for in that case palpitation may become progressively severe and can cause much distress.

Frequently, palpitation associated with premature beats can cause sensations in the *neck* and in the *head*. One of the best descriptions of such subjective sensations was given me by a fourth year medical student who suffered from rheumatic aortic insufficiency with a superimposed, eventually fatal, sub-acute bacterial endocarditis. "The extra systole has always affected me as if it were a cannon ball, shot point blank at my brain. The sensation is that of a terrific explosion occurring



within the narrow and limited confines of a calcified skull, which refuses to yield to the compressive force. It is like an irresistible force against an immovable object. Most of the time I am helpless before it and simply wait patiently in terror until the ordeal has passed. I have never been able to satisfy myself as to why I never suffered the sequela of a cerebral accident following an extra systole, for I can think of no other sensation which can so closely simulate breaking of any blood vessel in the brain without doing so."

Palpitation is a symptom, which like other symptoms of the diseased heart, occurs both in health and in disease. The interpretation depends on the underlying condition of the heart. If a patient complains of palpitation, even at rest, and examination fails to reveal evidence of organic heart disease, then nervous disturbances, smoking or other intoxications, or transient arrhythmia should be suspected.

#### THORACIC SORENESS, ACHE AND PAIN

Unpleasant or painful sensations are the most characteristic symptoms originating from the heart or its great vessels in disease or physiologic stress. These sensations are usually localized in various parts of the thorax ("dolor pectoris"), but, as a result of visceral-reflex radiations, they can also be referred to regions distant from the heart, such as the upper extremities, neck, head, epigastrium, abdomen and even the lower extremities.

Cardiac pain is one of the extensively studied symptoms of the heart, yet its mechanism is but partially understood. The interpretation of this symptom requires great clinical acumen, because not every cardiac pain is angina pectoris, nor does cardiac pain necessarily indicate structural disease. "Dolor cordis" has no specific differential characteristics. Thoracic injuries, neuralgias, mediastinal infections, ruptured bullae in emphysema, pleurisy, embolism, diverticula and ulcers of the esophagus, and diseases of various abdominal viscera, particularly those of the stomach, gallbladder and pancreas, can give rise to painful sensations similar to or identical with those

originating from the heart. The proper diagnosis of cardiac pain depends on bringing the characteristics of the pain (intensity, location, radiation, duration and periodicity) into proper relation to other clinical findings, particularly the *precipitating factors*.

**Dull Precordial Distress (Heart Ache).**—Because dull precordial distress, with or without tenderness or hyperesthesia, is a common symptom in patients without heart disease, and because to most persons the heart is a symbol of life and death, this sensation is responsible for much mental anguish, hidden or admitted. Many otherwise healthy persons consult physicians because of precordial distress or hypersensitivity, and many hypersensitive, introspective persons with normal or hyperirritable hearts develop such *heart ache*. In some of these persons the heart ache is but a projected symptom of the psyche or an hysterical conversion manifestation symbolizing conscious or subconscious psychic experiences (*cardiac neurosis*). Again, there are others in whom heart ache is a physiologic symptom of a somewhat inefficient and hyperirritable cardiovascular system (*soldier's heart, neurocirculatory asthenia, nervous heart*). The same type of precordial distress is frequently experienced by robust persons after chronic fatigue or severe physical exertion (*heart ache of fatigue*). Naturally, patients with heart disease, particularly if they are introspective, will complain of this precordial ache.

There are several clinical characteristics of this type of distress or pain which *differentiate* it from the *pain of angina pectoris* or *coronary thrombosis*. In contrast to the pain of angina pectoris, which in the majority of instances is localized in the midsternum or slightly to the left, the dull "heart ache" is located over the precordium, often over the apex or the supracardiac area on the left side. Frequently there is heart ache and some degree of hyperesthesia over the corresponding area on the right. Such contralateral hyperesthesia is not usually present in angina pectoris. Further, in contrast to the pain of angina, which lasts but a few seconds or minutes, the "heart ache" frequently lasts for hours. At times, patients

with "nervous heart ache" complain of severe lancinating pain or "stabs" lasting but a second or fraction of a second. This may return at irregular intervals and alarm the patient. Radiation of the pain is not an absolute differential point, because in cardiac neurosis or following severe exertion the precordial pain may radiate to the left arm, as in angina pectoris. Patients with such radiating pain but without organic heart disease may cause much difficulty to inexperienced physicians, and the correct interpretation of this type of distress or ache will depend again on the full consideration of the patient as a psychophysical unit.

Mild or severe dull, nonradiating precordial pain can be associated also with any type of organic heart disease with dilatation of the chambers. Pericardial effusion or fibrinous pericarditis, in my experience, usually causes such nonradiating pain. At times the pain is referred to the epigastrium, and in some cases with fibrinous pericarditis it is referred to the second or third costal interspace just to the left of the sternum—often an area where the friction rub is the loudest.

**The Pain of Angina Pectoris.**—The paroxysmal substernal oppression or pain of angina pectoris has several characteristics which, together with other clinical findings, allow the diagnosis of this condition with a high degree of accuracy. Angina pectoris is a clinical concept based on transient physiological changes in the coronary circulation. It should be considered as a syndrome, depending on a transient insufficiency in the oxygen supply of the myocardium. Local changes within the coronary vessels play an important predisposing rôle in the causation of pain. The underlying structural or physiological states which predispose to the syndrome or are responsible for it are numerous. Diseases of the coronary arteries are but one type of structural alteration of the heart, which can be associated with angina pectoris (*Heberden's angina pectoris*). Other cardiac disorders prone to be associated with angina are aortic insufficiency, aortic stenosis, advanced mitral stenosis, cardiac hypertrophy associated with arterial hypertension, hyperthyroidism, anemia and paroxysmal

tachycardias. In these disorders the coronary artery is frequently normal, and the syndrome of angina pectoris depends primarily on physiologic disturbance of the coronary blood flow as conditioned by the underlying alteration in the heart or general circulation.

*Character of the Pain.*—Some physicians diagnose angina pectoris only if the paroxysmal pain is severe, although actually in many instances in the early stage of the condition the distress is mild and lasts but a few seconds. At this stage, which may persist for years, there may be merely a little sub-sternal or epigastric distress, "twinge," fulness, choking, pressure or indigestion which is relieved by belching. The patient is slightly apprehensive, but before he fully appreciates the situation the attack is over. In more severe cases the distress or pain is felt near the midline anywhere from the epigastrium to the manubrium. The pain may radiate along the arm to the finger tips, generally to the left but occasionally to the right. The radiation may be continuous or may skip certain regions. In some patients the radiation involves the neck, jaw, face, back and other areas. At times the pain may be localized over distant areas without thoracic distress. Such pain is precipitated by the same factors as the typical pain. The pain of angina may masquerade as "arthritis" of the shoulder or the wrist. Rarely the pain exhibits "inverse radiation" originating in the left arm or other structure and radiating to the sternum. Under certain circumstances a given type of radiation of some years' duration can suddenly change.

*Associated Symptoms.*—The typical attack of angina pectoris is associated with anxiety or *angor animi*. Frequently, profuse perspiration with pallor or flushing is present; the clothes may feel tight, and strenuous effort may be made to loosen the collar. In some cases, attacks of angina are associated with paroxysmal dyspnea and asthma. The duration of even severe attacks rarely exceeds five to ten minutes.

*Differential Diagnosis.*—Patients suffering from angina frequently experience the dull precordial pain or pressure, described previously, independent of the pain of angina. The

two types of pain should be differentiated, or the syndrome is confusing. The pain or distress of angina is characteristically precipitated by physical exertion, mental anguish and food. Frequently, when the patient is worried, very slight exertion will bring on an attack, and similarly consumption of food increases the likelihood of attacks precipitated by work. I have observed a patient whose occupation was reading gas meters, and who discovered that he could perform his duties only if he took no meals until the afternoon, when his work for the day was finished. Breakfast alone was sufficient to cause repeated attacks of angina, if he attempted his usual work.

*Prognosis.*—The attack of anginal pain is relieved quickly if the patient remains immobile in the upright position. Polyuria and deep sleep may follow relief. Although no conclusions as to prognosis can be drawn from the intensity of the attacks, since even mild attacks may be soon followed by sudden death, on the whole the more severe and prolonged the attack, the worse the prognosis. In the interpretation of symptoms and in the prognosis, the underlying causative mechanism is an important consideration. Obviously, a patient with hypertension and severe anemia may suffer from severe attacks of angina, and yet, following the treatment of the anemia, the angina may subside.

The *pathogenesis* of the pain of angina pectoris is outside the scope of this discussion. It is believed today that the stimulus for the pain is a metabolite which is prone to accumulate in the tissues (muscle and vessel wall) in the presence of anoxia. Clinical and experimental findings indicate that the work of the heart and the blood supply are the factors upon which the presence of the suspected metabolite depends. Some evidence supports the suspicion that the causative agent acting on the nerve endings in the heart is an organic acid. The afferent impulse from the cardiac nerve endings travels mainly via the sympathetic nerves and via the first four or five dorsal rami communicantes to the central nervous system.

In the production and radiation of pain, viscerocutaneous

reflexes play an important rôle. This is attested also by the fact that such referred pain can be abolished by intracutaneous infiltration of the affected areas with novocain solution. Following this anesthesia, however, the pain may be referred to other cutaneous regions. We have observed this "migration of the pain," also, in instances of referred pain originating in other viscera, and the migration has been studied experimentally in pain originating in various portions of the esophagus distended with an inflated balloon. With the inhibition of the original pain, the new radiation is influenced by the presence of irritable foci located in nearby spinal segments. Similar migration of anginal pain has been observed after surgical sympathetic nerve section, as demonstrated by the following case:

A. F., a fifty-six-year-old man, had suffered from severe daily attacks of anginal pain since December, 1939. The pain was squeezing-stretching in character and located in the midsternum, radiating to the left shoulder, hand, and fingers. Since February, 1940, the attacks had become more severe, occurring even at night, and as often as 10 to 15 times in twenty-four hours. The attacks were usually preceded by exertion connected with talking, anger, the effort of walking, dreams related to his work and consumption of food, and they were relieved by nitroglycerin. The pertinent findings were an enlarged heart with accentuated aortic second sound; arterial pressure rising from 170/110 mm. of mercury at rest to 240/150 mm. during the attack; and inversion of the T wave of the IV lead of the electrocardiogram.

As a therapeutic measure, left cervical sympathectomy, with removal of the first and second dorsal ganglia, was performed by Dr. E. C. Cutler. For five days following operation no attacks were experienced. On the sixth post-operative day a nonradiating, burning, epigastric pain just below the xiphoid process, unexperienced heretofore, appeared. These attacks of distress, partially relieved on belching, developed with increasing frequency, and were induced by the same type of stimuli as the previous typical radiating pain, and were likewise relieved by nitroglycerin. In one of these attacks two weeks after operation the arterial pressure rose from 140/100 mm. of mercury at rest to 180/120 during the epigastric episode.

It should be remembered also that *migration of pain* in angina occurs not only after section of the nerve paths or cutaneous anesthesia, but also as a result of the development of a new "irritable focus." Thus, anginal pain which has radiated to the arms for years, may change its radiation to the jaw as the result of the presence of an abscessed tooth. I have

observed anginal pain change its usual radiation from the sternum along the left arm, to the left lumbar area, following the development of an acute left-sided pyelonephritis.

**The Pain of Coronary Thrombosis.**—This pain has many of the characteristics of that in angina pectoris. This is to be expected in view of the fact that coronary sclerosis is both the most frequent lesion underlying angina pectoris and the most frequent cause of coronary thrombosis. Indeed, in many instances coronary thrombosis is but the end-result of angina.

*Character of the Pain.*—The degree of pain varies from a mild, dull sensation to a severe, unbearable, and excruciating pain, frequently in the form of a vice-like, squeezing, crushing agony. The localization is essentially the same as in angina pectoris. The main differential characteristics are the longer duration and the lack of relief from nitroglycerin in coronary thrombosis. In the latter disease the pain lasts for hours or days, but during these long periods many patients experience marked fluctuation in its severity.

*Associated Symptoms.*—The associated vasomotor disturbances are more intense than those in angina. Dyspnea, asthma, pulmonary edema and vomiting may accompany the more severe attacks. Often there is also a sense of impending dissolution. Temporary disturbance of the cutaneous sensation along the area of the radiation of the pain may develop.

*Differential Diagnosis.*—Rarely the pain may be abdominal and may imitate that of surgical emergencies. Although, in the typical instance, the diagnosis of coronary thrombosis is made without difficulty, in many instances a definite diagnosis cannot be established. Pain originating from a number of organs other than the heart can have the same character as that of coronary thrombosis. Certain types of disturbance of the coronary circulation associated with prolonged pain and electrocardiographic changes are incorrectly diagnosed as coronary thrombosis. Contrariwise, some short attacks of pain without electrocardiographic changes, considered as transient attacks of angina, are caused by thrombosis of minute branches of the coronary arteries.

It is misleading to attempt to separate too rigidly different types of pain in different types of heart disease. While statistically the type of pain in rheumatic pericarditis, mitral stenosis and syphilitic or dissecting aneurysm varies; in individual cases the difference frequently is vague.

Venous congestion of the *liver* can cause epigastric or *right upper quadrant distress and tenderness*. In some hypersensitive patients the pain of hepatic origin can become so intense that acute abdominal emergency is suspected. In my experience this occurs most frequently in acute decompensation in relatively young patients who suffer from rheumatic heart disease associated with mitral or tricuspid stenosis. In some patients one is unable to find a relationship between the severity of distress on the one hand and enlargement of the liver or increased venous pressure on the other hand. Ascites can be responsible for annoying pressure sensations. In patients with tricuspid stenosis the prominence of abdominal symptoms associated with high venous pressure and a relatively slight degree of dyspnea is a useful diagnostic aid. Excessive edema of the lower extremities can cause a sensation of tightness. Such patients have a tendency to painful cutaneous (erysipeloid) infections.

#### BREATHLESSNESS (DYSPNEA), ORTHOPNEA, ASTHMA AND COUGH

Symptoms referable to the respiration and to the physiologic state of the lungs are the most common manifestations of heart disease. They are also the most useful aids in estimating the cardiac reserve and degree of cardiac failure. One can judge the state of the circulation more accurately by correctly interpreting these symptoms than he can on the basis of any observations made with tests and instruments. But such an evaluation requires proper physiologic and clinical knowledge.

**Dyspnea.**—Breathlessness is induced in normal persons by physical exercise, and many states of the body within the normal range predispose to this condition. Thus, dyspnea of obesity, depending mainly on insufficient function of the diaph-



ragm, can develop as easily on slight physical exertion as dyspnea associated with heart disease. Breathlessness is caused also by diseases of the pleura, lungs, bronchi and mediastinum. Contrary to a frequently expressed view, dyspnea is not an early symptom of all types of heart disease. For example, in diseases of the coronary arteries, of the right ventricle, of the pericardium and in pure tricuspid stenosis, dyspnea and related symptoms frequently either do not appear or are relatively late manifestations.

In the interpretation of respiratory symptoms in cardiac patients one must take into consideration the type of the underlying heart disease; the presence of independent disease or physiologic states of the pleura, lungs, mediastinum and diaphragm; and the nature, intensity and duration of the stimuli which precipitate the dyspnea. In the prognosis, the progressive change in the severity of the stimuli causing dyspnea is a helpful guide.

Dyspnea is one of the first symptoms of diseases of the mitral valve, the left ventricle and the aortic valve, because in these conditions the inflow or the output of the ventricle is disturbed and pulmonary engorgement develops quite early. In the *pathogenesis of dyspnea*, orthopnea, asthma and cough of cardiac origin, pulmonary changes and secondary reflex stimulation of the respiratory center play the chief rôle. These pulmonary changes consist of active or passive engorgement of the pulmonary circuit, pericapillary and intra-alveolar edema, and pleural effusion. Even when the volume of blood flow is unaltered, the velocity of the pulmonary circulation is considerably slowed down, indicating the increase in the diameter of the capillaries shown in histologic studies. The combination of these changes lead to stiffening of the alveolar wall and reduction of the elasticity of the vital capacity of the lungs. In addition to the absolute reduction of the air spaces caused by the increased amount of blood and transudates, there is also physiologic emphysema of the lungs. Hence the absolute reduction of the vital capacity is greater than that indicated by the volume of accumulated fluids. While all the

pulmonary changes responsible for cardiac dyspnea and related symptoms are physiologic (reversible) in their origin, they can result in permanent structural changes. As we have demonstrated in cases of mitral stenosis, thickening of the basement membrane, deposition of collagen, and swelling of the flat epithelial cells of the alveolar wall can develop eventually.

The simplest clinical demonstration of the fact that in cardiac dyspnea the primary factors are the pulmonary-medullary reflexes, and not chemical changes in the blood supplying the respiratory center (anoxia, acidosis, or congestion of the respiratory center), is offered by the contrast in the behavior of patients with hypertensive heart disease and aortic insufficiency on the one hand, and constrictive pericarditis and thrombosis of the vena cava superior on the other hand. In the first group with evidence of pulmonary engorgement, dyspnea is a prominent symptom and can be present even at rest, at a stage of circulatory failure in which the venous pressure, the hemodynamics of the greater circulation and the chemistry of the arterial blood are normal. However, little or no dyspnea is manifested in cases of constrictive pericarditis or thrombosis of the vena cava superior with high venous pressure and presumably slow flow through and congestion of the respiratory center, but without pulmonary congestion. Since 1931 we have emphasized these facts and concluded that failure of either of the two circulations (peripheral or pulmonary) can develop to a large extent independently of the other. As attested also by chemical and physiologic studies, failure of the pulmonary circulation with secondary hyperactivity of pulmonary-medullary reflexes is the most important single cause of cardiac dyspnea. In certain instances of heart disease, however, chemical changes also play a part. The rôle of the reflexes originating in distended auricles or in the large veins of the heart cannot be estimated at present. It is of interest that patients with rheumatic fever, who have an unusually large left or right auricle reaching a capacity of one liter or more, suffer from relatively little dyspnea. Physiologic studies indicate

that important reflexes can originate from the root of the large cardiac veins, but the clinical significance of these reflexes is obscure at present.

The usual form of cardiac breathlessness is precipitated not only by physical exertion, but also by nervous strain and eating. The more severe the cardiac changes, the less intense the stimulus needed to precipitate shortness of breath, and a stage may finally be reached in which dyspnea occurs even at rest. Pain and other factors which stimulate the respiratory center can accentuate cardiac dyspnea.

It is of interest that voluntarily or centrally induced *rapid breathing (tachypnea)* is especially apt to induce the sensation of dyspnea in patients with pulmonary engorgement due to heart disease. Thus we have frequently had the opportunity to observe that tachypnea caused by intravenous administration of physiologic doses of sodium cyanide, in contrast to the behavior of normal persons, precipitates dyspnea and orthopnea in cardiac patients at rest. There is a relationship between the severity of the pulmonary disturbance and the ease with which a certain degree of tachypnea can cause dyspnea.

A somewhat similar relationship exists between periodic apnea and hyperpnea (*Cheyne-Stokes respiration*) and the sensation of dyspnea. Cheyne-Stokes respiration can occur in normal persons in sleep, particularly after extreme fatigue or certain medications, and can also be present in many diseases. Under most of these conditions it causes no dyspnea. In patients with heart disease and in the presence of "left ventricular failure," however, Cheyne-Stokes respiration is common, and can be the source of a severe degree of breathlessness and orthopnea. It is a common experience to observe a patient with left ventricular failure and pulmonary engorgement who, periodically with each phase of hyperpnea and dyspnea, awakens in terror of dyspnea and then slumbers in deep sleep.

Because cardiac dyspnea is pulmonary in origin, it can be used as a measure of heart failure only if other disturbances of the lungs and respiration do not exist or are properly evaluated. Among factors which reduce the vital capacity of

the lungs and the economic function of the respiration and accentuate cardiac dyspnea the most common are *pulmonary emphysema and bronchitis*. These conditions *per se* are responsible for dyspnea, and hence in their presence heart failure will intensify the breathlessness. In such patients one must distinguish between the part played by heart disease and that played by the pulmonary disease. Such evaluation is important also to the proper estimation of prognosis. Everything being equal, the same degree of dyspnea associated with co-existent heart disease and emphysema offers a better prognosis than with heart disease alone. In my experience, acute bronchitis in the presence of mitral stenosis is particularly disposed to accentuate dyspnea.

Obesity, abdominal fluid, and disease of the stomach, gall-bladder and common duct are conditions which mechanically or reflexly interfere with the function of the diaphragm and accentuate the dyspnea caused by heart disease.

Aneurysm of the aorta *per se* causes dyspnea only if it presses on the trachea, bronchi or lung, possibly resulting in collapse of the lung. Otherwise the dyspnea associated with *aneurysm of the aorta* or with *syphilitic aortitis* is cardiac in origin, depending usually on an associated narrowing or occlusion of the coronary orifices or an aortic insufficiency and secondary left ventricular failure. Valid evidence is not available that syphilitic involvement of the root of the aorta causes reflex dyspnea through irritation of nerve endings within the wall of the aorta. An instructive clinical demonstration of the fact that irritation of the nerve endings of the aortic arch does not cause reflex dyspnea is afforded by the behavior of patients at the onset of dissecting aneurysm of the aorta. In these persons, dyspnea is absent or slight, although the coats of the aorta are ripped from the valve to the iliac artery. I was unable to induce reflex dyspnea in dogs by mechanical irritation or tears of the root of the aorta effected by instruments introduced into the aorta through the carotid arteries.

Some persons complain of "shortness of breath," but proper questioning reveals that this symptom depends on *periodic*

*sighing*. Such frequent periodic sighing with the sensation of breathlessness is not a symptom of heart disease, but usually a complaint of hypersensitive and neurotic persons or of the cardiac patient with superimposed neurosis.

**Orthopnea.**—This is a special type of dyspnea which is closely related to the usual dyspnea caused by pulmonary congestion. Patients who suffer from pronounced dyspnea caused by pulmonary engorgement and related changes usually seek a position (*orthopnea of choice*) in which dyspnea is not experienced, and prefer to rest or sleep in a semirecumbent rather than a horizontal position. If the trunk of a patient with pronounced orthopnea is lowered from the position of "choice," an angle is reached below which the patient cannot tolerate the distress of breathlessness (*orthopnea of necessity*).

Just as in dyspnea on exertion, so in orthopnea a strict parallelism between the degree of heart failure or pulmonary congestion and the degree of orthopnea does not exist, because orthopnea, too, is a subjective sensation, and individual variation in the reflex sensitivity of the central nervous system is a determining factor. Orthopnea, for obvious reasons, appears later than dyspnea on exertion. "Dyspnea at rest" caused by heart disease is a relative state, because it depends on the position of the body. A patient experiences "dyspnea at rest" when in a position below the angle of orthopnea, but he is free of dyspnea when resting above that angle; and only if the trunk is in the upright position can we speak of "absolute dyspnea at rest."

It should be added, however, that many cardiac patients who experience dyspnea in the sitting position will be relieved of their dyspnea when standing in an immobile position. This is due mainly to better function of the diaphragm and to improvement in the cardiac work and the pulmonary congestion, as a result of the stagnation of blood in the dependent portion of the venous system which occurs when the patient stands motionless.

Orthopnea depends primarily on *active stimulation of pulmonary reflexes* by engorgement and secondary changes in the

alveolar walls. Reduced vital capacity has an important bearing on orthopnea, but alone is not an explanation for the condition. The vital capacity of the lungs changes but little or not at all below and above the level of orthopnea of choice or necessity. It should be remembered, however, that the same volume of blood flows through the lungs under different pressure relations in different positions of the thorax. Thus, in the recumbent position a large portion of the lungs is below the level of the auricles; and the pulmonary venous pressure in these portions must be relatively high, adding to the work of the right heart. In the sitting position the pressure relations and the hemodynamics within the pulmonary circuit are improved. It is of interest to note that some patients with severe dyspnea and orthopnea at rest experience the greatest relief in bed when bending forward. In this position a relatively small portion of the lungs is in the dependent position and at the same time pressure on the inferior vena cava aids in shunting blood to the periphery, thereby reducing the circulating blood volume. In this position, pressure by an enlarged heart on the pulmonary structure may also improve.

Orthopnea is not caused by increased peripheral venous pressure and secondary congestion of the respiratory center. This conclusion is supported not only by the results of physiologic studies, but also by the following *clinical observations*: (1) Severe and characteristic orthopnea occurs when pulmonary engorgement caused by heart disease exists, even if the venous pressure and the hemodynamics of the larger circulation are normal. (2) Orthopnea is also caused by pulmonary disturbances of noncardiac origin, with normal peripheral venous pressure. (3) Thrombosis of the superior vena cava or constrictive pericarditis is associated with unusually high venous pressure, and yet these patients with distended veins in the forehead do not experience orthopnea. (4) Similarly, normal persons in whom high cerebral venous pressure is induced by sudden obstruction of the veins of the neck do not experience it. (5) The fact that elevation of the head relieves a somewhat unpleasant sensation in the head caused by high venous pres-

sure, which is not orthopnea, does not bear on the mechanism of orthopnea. This change in sensation cannot be offered, however, as evidence to support the concept that venous engorgement of the respiratory center is responsible for orthopnea, because it does not occur regularly, and it is observed also in patients with severe orthopnea but with *normal venous pressure*. More probably the effort of bending the head forward is related to changes in the position of the trachea, bronchi, and their accompanying nerves.

In the evaluation of the significance of orthopnea as a symptom of heart disease, other noncardiac factors must be considered in the same manner as in cardiac dyspnea.

**Paroxysmal Dyspnea (Cardiac Asthma).**—Paroxysms of dyspnea occur usually in patients with hypertensive heart disease, coronary insufficiency such as that caused by arteriosclerosis or luetic aortitis, aortic stenosis and insufficiency, and rarely mitral stenosis. They are the most striking feature of the syndrome of left-sided failure of the heart. In contrast to the usual type of dyspnea, cardiac asthma often occurs at rest, especially during the night. It is a seizure which can jeopardize the life of a patient who, between the attacks, is comfortable and possesses good or fair cardiac reserve. This type of paroxysmal dyspnea is prone to be severe in patients with reduced elasticity of the lungs, like that found in emphysema. The majority of patients with a tendency to cardiac asthma show reduced vital capacity and engorgement of the pulmonary circulation before the onset of attacks, but the hemodynamics of the greater circulation can be normal. The attacks depend on sudden and very transient *failure of the left side of the heart* due either to elevated arterial pressure or increased venous return, or a combination of the two. As a result of this temporary imbalance, several hundred cubic centimeters of blood can be trapped in the lungs between the two sides of the heart; and thus this dyspnea may be said to depend on an acute pulmonary hypertension and engorgement. Although the balance between the two ventricles is promptly reestablished, and thereafter the stroke volume of both ventricles is again equal, severe

dyspnea, congestion and pulmonary edema associated with terror persist as long as the trapped blood is not eliminated.

In many of the patients a bronchospastic element (*asthma*) predominates in the clinical picture. Patients with a past history of bronchial asthma or bronchitis are very likely to have a severe bronchial-asthmatic element with the paroxysmal dyspnea. In the precipitation of attacks the horizontal position of the body, excitement, nightmares, eating and physical exertion are involved. Any factor—pleural fluids and ascites or Cheyne-Stokes respiration—which reduces the lung volume increases the tendency to the paroxysms. Paroxysmal dyspnea of cardiac origin offers a serious prognosis even if, between the attacks, the patient is capable of doing his usual work.

At times the differentiation between attacks of asthmatic bronchitis and cardiac asthma is difficult, and both conditions may coexist. In many respects the mechanisms of paroxysmal dyspnea is the same as that of the usual continuous cardiac dyspnea, the main difference being the time element. In cardiac asthma the factors develop suddenly within seconds or minutes, while in the usual dyspnea it takes months or years.

**Dyspnea in the Aged after Prolonged Bed Rest.**—There is a type of dyspnea, which so far as I know, has received little attention, and which is associated particularly with coronary disease. This occurs in elderly persons and may appear for the first time after prolonged bed rest. It is a manifestation of congestive heart failure induced by rest ("*paradoxical cardiac failure*"). Judging from fairly extensive experience, the ischemic myocardium tends to adapt itself to a minimal amount of essential cardiac work, with the result that during bed rest, in the absence of the stimulus of accustomed exercise, the cardiac reserve decreases. In these patients, too, there is a tendency to hypostatic pulmonary congestion. Hence, when they are allowed to leave their beds, symptoms and signs of congestive failure with dyspnea appear even on very slight exertion. In some patients the heart acquires its former functional capacity only after gradual institution of prolonged exercise. The behavior of these patients demonstrates the fact that



prolonged bed rest can be harmful. This is true, too, in certain patients with left ventricular failure, who have been up and about, and for whom absolute bed rest leads within a few days to intense dyspnea and, at times, to hydrothorax and bronchopneumonia.

**Dyspnea Secondary to Water Retention.**—In patients with a tendency to water retention like that in *glomerulonephritis*, *preeclampsia*, *eclampsia* and *beriberi*, there is a tendency to dyspnea on exertion, to orthopnea, and to paroxysmal dyspnea (cardiac asthma). The evaluation of the pathogenesis of these dyspneas requires special consideration. In each of these conditions there may be a cardiac element, but frequently the tendency to water retention also causes the lungs to become water-logged and the respiratory function to become impaired. Varying degrees of acidosis may also be associated with the severe forms of these diseases. These three factors (cardiac damage, water retention in the lungs, and acidosis) in various combinations can contribute to the three types of dyspnea. Because the changes leading to dyspnea can occur within a short period, patients with good or fairly good functional capacity of the heart can develop dyspnea on exertion, continuous dyspnea, orthopnea or asthma with unexpected rapidity.

If cardiac patients develop *circulatory collapse and shock*, intense dyspnea may result from associated pulmonary edema, which depends on increased capillary permeability rather than on pericapillary edema.

**Cough.**—Cough is a common complaint of some cardiac patients, and this is not surprising considering the disturbances in the pulmonary circulation in congestive heart failure. The cough may occur in single bouts or in long paroxysms. Nocturnal paroxysmal cough is frequently the forerunner of typical attacks of paroxysmal dyspnea. Pressure on the trachea or displacement of the bronchi by the large auricle can cause cough without congestive failure. In patients with chronic left ventricular failure, particularly that caused by arterial hypertension, chronic increased bronchial secretion is responsible for a constant, annoying cough, most disturbing at night.

Some of the bronchi become plugged by tenacious secretion, and the patient may struggle and cough for hours before succeeding in removing the mucous secretion. This type of cough often precipitates cardiac asthma. A peculiar short, hacking, irritating and nonproductive cough can be present with rheumatic pericarditis.

The mechanism of the cardiac cough is essentially the same as that of any other cough. It is a medullary reflex phenomenon, and the efferent impulses can arise from a number of areas: the lungs, the bronchi or trachea, or the higher sensitive regions when the irritating secretions reach them. It is important for physicians to avoid the erroneous diagnosis of cardiac cough as bronchitis or "colds."

#### WEAKNESS AND EXHAUSTION

These are common symptoms of heart disease, and may be early manifestations of impaired cardiac reserve. These patients complain of complete exhaustion at the end of their usual daily work, long before the more specific sensation of dyspnea is experienced. Weakness may be a prominent complaint in acute rheumatic carditis without failure. Weakness in the morning is a regular complaint of cardiac patients with arterial hypertension, but this symptom is related to the hypertension. In the more pronounced stage of heart failure, weakness, resulting from the summation of several disturbances, is a regular complaint. In the so-called "effort syndrome," weakness and rapid heart action are the main complaints.

#### HEADACHE AND INSOMNIA

Headache is not an outstanding symptom of heart disease, although in some patients with aortic insufficiency it can be a prominent complaint. The headache of patients with hypertension is vascular and not cardiac in its origin. Insomnia becomes prominent usually only in the presence of congestive failure, though at times it is associated with coronary sclerosis or thrombosis even without congestive failure. It is caused by

various disturbances such as Cheyne-Stokes breathing, mild attacks of nocturnal dyspnea, and nightmares. In many patients with coronary disease, unexplained anxiety, emotional outbursts and prominent changes in the personality are common. One should think of silent coronary thrombosis, if a calm person suddenly develops personality changes of obscure origin.

In patients with hypertensive or coronary disease *sleeplessness* is often caused by nocturnal *Cheyne-Stokes breathing*. Even in patients with only mild dyspnea on exertion, Cheyne-Stokes respiration is frequently present during sleep. In many patients, particularly in the early stage of their heart failure, Cheyne-Stokes respiration and the associated "nervousness" and "restlessness" occur for but an hour or two after retiring. In the more advanced stage of pulmonary congestion, however, the periodic breathing can be responsible for prolonged nocturnal nervousness, terror and nightmare. Sedation may accentuate Cheyne-Stokes respiration.

#### ANOREXIA, NAUSEA AND VOMITING

Normal appetite is a sensitive index of good health, for most illnesses, even of a mild nature, are accompanied by anorexia. It is natural, therefore, to find that, in the presence of congestive failure, *anorexia* is common. *Belching of gas* and *flatulence* with abdominal distention are likewise frequent. These symptoms are present in coronary disease without congestive failure.

It should be remembered that a reversible medullary reflex interrelationship exists between the heart and the stomach, and that *nausea and vomiting* are not rare as symptoms of cardiac disturbance. They result reflexly from several viscera. Coronary infarction is quite frequently accompanied by vomiting. Marked passive congestion of the viscera also can be responsible for nausea and vomiting. *Digitalis* and *morphine* are the two drugs which in the course of the treatment of heart

disease most frequently precipitate attacks of vomiting. The separation of vomiting caused by heart disease or congestion and that caused by medication may be difficult. The vomiting induced by digitalis is a reflex reaction originating in the heart. The afferent impulses travel to the vomiting center in the medulla both through the sympathetic nerves via the cord and through the vagus nerves. It is probable that the vomiting of cardiac infarction has a similar mechanism. The vomiting caused by morphine is central in origin. *Mental depression* in association with even a slight degree of nausea is not uncommon. *Hiccup* is a symptom of serious significance in patients with cardiac infarction. It can be caused by morphine. *Diarrhea* can be an equivalent manifestation with vomiting. It should be appreciated, too, that mild nausea may be associated with epigastric distress or pain.

#### GIDDINESS AND FAINTING

Giddiness, "lightheadedness," and fainting are fairly frequent symptoms in patients with certain types of cardiac disturbances. In general, giddiness occurs more frequently than fainting, because the former is a "forme fruste" manifestation of cardiac syncope. Syncope of the vasovagal type is prone to occur in patients with circulatory asthenia when standing motionless, particularly after severe exertion. Similarly, after prolonged bed rest cardiac patients are apt to experience spells of giddiness and fainting, which in the presence of severe myocardial disease may be associated with convulsions and other severe disturbances of the central nervous system.

Among the valvular diseases, advanced mitral and aortic stenosis are prone to be associated with giddiness and fainting. The syncope of *aortic stenosis* depends probably on vagal hyperirritability of the myocardium, as a result of myocardial ischemia, and is not of carotid sinus origin. The fainting may occur at rest or on exertion. The prognostic significance of attacks of syncope in aortic stenosis lies in the fact that it carries with it a certain degree of statistical predisposition to

instantaneous death (fatal syncope). The fainting associated with *mitral stenosis* results primarily from impaired cardiac output due to the mechanical obstruction to the blood flow introduced by the diseased mitral valve. For this reason, this type of giddiness and fainting is prone to occur during or immediately following exertion. In my experience the tendency to faint becomes accentuated during pregnancy in these patients.

The onset of *coronary thrombosis* may be signalled by a fainting spell. Indeed, syncope may be, at times, the only symptom of coronary thrombosis. In general, in persons over forty years of age with no past history of fainting spells, an attack of syncope without obvious causes should be considered as having possible grave significance. Following coronary thrombosis the ischemic myocardium becomes hyperirritable, and attacks of giddiness and fainting are experienced fairly frequently by some patients.

Myocardial anoxia caused by coronary sclerosis is responsible for myocardial hyperirritability to vagal impulses and other stimuli. Hence, patients with *coronary disease* are in general predisposed to transient myocardial standstill and irregularities and to secondary giddiness or fainting. These changes can be precipitated by various types of vagal reflexes, including that originating in the carotid sinus. It is for this reason that patients with coronary disease are prone to develop syncope, which may end fatally, during pleural, peritoneal or pericardial taps.

Transient cardiac irregularities with rapid or slow rate which are frequently responsible for cerebral symptoms include premature ventricular beats, attacks of auricular fibrillation, auricular or ventricular tachycardias, and complete auriculo-ventricular dissociation.

#### HOARSENESS

This is not a common symptom in heart disease, but may be caused by a large auricle which, like aneurysm of the aorta, exerts pressure on the recurrent laryngeal nerve.

## CHILLS AND FEVERISHNESS

*Chill* is a symptom of heart disease only in cases of acute or subacute bacterial endocarditis, purulent pericarditis, and myocardial abscess, and is usually not associated with severe congestive failure. I have gained the impression that severe congestive failure abolishes at least to some extent the capacity for chills; a conclusion which is in agreement with the observation that such patients behave somewhat like poikilothermic animals in their reactions to considerable fluctuation in the surrounding temperature. In the mechanism of chills, which is one of the important factors in temperature regulation, afferent sympathetic impulses from the skin, certain posterior hypothalamic centers, and extrapyramidal afferent pathways via the cord play a rôle. The nature of the physiologic disturbance of the temperature regulation in congestive failure is not well understood at present.

A *sensation of warmth or feverishness* is a frequent complaint in cardiac patients in acute distress, but it is frequently subjective, unassociated with fever. Thus, patients suffering from paroxysmal dyspnea, pulmonary edema or coronary pain may complain of unbearable heat and perspiration when the temperature of their surroundings and of their body is normal. If patients with heart disease actually have fever, this is also accompanied by the sensation of warmth, and is caused in general by the same factors which induce it in healthy persons. Because of impaired peripheral circulation in patients with severe congestive failure, the capacity for heat dissipation is impaired, and in warm surroundings the body temperature tends to become elevated. In the presence of tachycardia even without congestive failure some patients develop fever. The mechanism of this fever is not clear to me. Obscure fever without paroxysmal tachycardia and in surroundings of normal temperature is often due to bronchopneumonia or infarcts. Cardiac patients with severe pulmonary congestion have a tendency to develop a type of focal bronchopneumonia, which is frequently not associated with changes in physical signs,

chills, or leukocytosis, and may be manifested only by the appearance of the patient and by "obscure" fever.

#### COLDNESS AND INTERMITTENT CLAUDICATION OF THE EXTREMITIES

The heat regulation of patients with severe congestive failure is impaired, and they complain of *coldness of the extremities* when exposed to moderately low temperatures. In my experience, patients with severe mitral stenosis are particularly prone to experience coldness of the extremities due to poor peripheral circulation. I have observed two young patients with mitral stenosis in whom progressive and symmetrical trophic disturbances of the toes leading to gangrene developed slowly, and in whom, on postmortem examination, cardiac thrombi, arterial emboli, and arteriosclerosis were not found. It was concluded that poor circulation of cardiac origin was responsible for the gangrene in these patients.

Painful *intermittent claudication of the extremities* is usually of vascular origin, but cardiac factors can accentuate or actually induce the symptoms. There is a certain degree of statistical coexistence of coronary sclerosis or thrombosis and arteriosclerosis of the lower extremities leading to intermittent claudication.

#### CONCLUSIONS

The clinical interpretation of symptoms of heart disease has been neglected in recent years. This is attested by the lack of adequate discussion in the literature, including textbooks. Correct interpretation of symptoms is the most valuable aid to the physician in diagnosis and prognosis. If the pathogenesis of symptoms is taken advantage of, better treatment of them will follow.

Rational treatment of symptoms of heart disease may be as important as the therapy of the etiologic causes. Relief of pain, prevention of vomiting or hiccup, and induction of restful sleep in a patient with cardiac infarction may be equivalent to saving the life of the patient.

On the basis of information accumulated on the mechanism of symptoms, we are able to probe with greater precision the morbid processes within the depths of the body. The contribution of clinical and experimental studies to the knowledge of the symptomatology of disease may be compared to the rôle of geophysics and its influence on classical geology. Just as the modern science of geophysics made possible a more exact interpretation of the surface findings of geology in relation to the depth of the earth, so physical and chemical methods in medicine have resulted in a more precise and useful interpretation of the symptoms of disease.





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### ELECTROCARDIOGRAPHY AND THE GENERAL PRACTITIONER

THE task of the general practitioner has changed markedly during the past generation. Whenever a new technic in diagnosis or treatment is devised, tested, and proved to be valuable it is his duty to incorporate it in his own practice whenever possible. If the procedure is too intricate and difficult or if it requires expert knowledge, it will remain a function of the specialist. However, as time goes on, greater simplification is taking place so that more and more can be carried out by the willing and energetic practitioner. It should not be necessary for the cardiologist to tap a chest in a patient's home once the diagnosis of hydrothorax is made, nor should a patient need to keep going to a hematologist for liver injections once the diagnosis of pernicious anemia has been made. The greatest difficulty that confronts the general practitioner is to select amongst his patients those that might require a detailed blood examination, others that need a basal metabolism, still others that require an x-ray of the gastro-intestinal tract, etc. He must be alert to pick out the right patients for the various procedures. This entails a knowledge of the kind of valuable information that might be obtained by the different types of examination.

In applying these ideas to the question of electrocardiography it is necessary to be familiar with the various clinical

conditions in which this method of examination may be helpful diagnostically or therapeutically. Although more and more physicians are doing their own electrocardiographic work, it will be a long time before most practitioners will be using such an apparatus themselves. In the main, they will need to call in a technician or some other physician to obtain and interpret the tracings. The main question that confronts them is, When is an electrocardiogram needed? It is an axiom that the more expert a man is in heart disease, the less he needs an electrocardiogram. As a corollary to this, one may add that the more one knows about electrocardiography the less he is dependent on it.

**When Is an Electrocardiogram Needed?**—In general, there are four sets of circumstances in which an electrocardiogram may be helpful to a general practitioner: The first is during an acute or subacute *infection* when the possibility of *rheumatic fever* arises. There are very few common febrile conditions in which characteristic electrocardiographic changes occur except in rheumatic fever and diphtheria. Secondly, all the types of *cardiac irregularities* can be clearly differentiated in the electrocardiogram. Thirdly, during *acute coronary thrombosis* and in *chronic coronary artery disease*, distinctive changes in the ventricular complexes are often detected. Finally, there is a *heterogeneous group* of less common conditions in which the electrocardiogram may be helpful indirectly in diagnosis.

**Rheumatic Fever.**—Let us discuss in greater detail the above four conditions illustrating clinical experience in the different groups. It is obvious that the physician does not need an electrocardiogram in every febrile case he sees. When the diagnosis is well established, no further useful information can be obtained by taking a heart tracing. If a patient has lobar pneumonia, typhoid fever, pulmonary tuberculosis, etc., there is no need of an electrocardiogram. It will show nothing unusual, or if it did (apart from arrhythmia), it would not significantly alter the diagnosis, prognosis, or treatment of the case. On the other hand, if the course of the illness remains *obscure*

and no satisfactory diagnosis has been established, then the electrocardiogram may furnish information that would aid in identifying the condition as an *atypical* rheumatic fever.

It is well known that rheumatic fever may run a peculiar course lacking the characteristic polyarthritis with rapid successive involvement of many joints. The choreic state, instead of taking the form of characteristic purposeless, twitching movements and grimaces that are familiar to all of us, may mask under the guise of slight nervousness or irritability. In fact, rheumatic fever may show neither rheumatic pains nor chorea and appear primarily as a sore throat followed by skin lesions of one sort or another, or with abdominal pain, nausea with or without vomiting. Or it may have no other distinctive features except slight or marked involvement of the heart. It may even lack the above symptoms and resemble tuberculosis because of loss of weight, sweats, fatigue, slight fever, etc.

It is in these *atypical* cases that the electrocardiogram may be helpful. The two changes to be sought for are *disturbances in conduction*, particularly first degree heart block (so-called delayed conduction time), and *alterations in the ventricular complex*. With the first change the P-R interval becomes prolonged beyond the normal 0.16 seconds for children and 0.2 seconds for adults. The second change is the development of a peculiar R-T segment in which the customary iso-electric R-T interval disappears and there may even be an elevated R-T interval crudely resembling the changes seen in acute coronary thrombosis. There are only a few other conditions that produce the first of the above changes, *i. e.*, delayed conduction. If digitalis had not been administered in recent weeks, if coronary artery disease can be ruled out, and if it is known that the condition is not congenital (as rarely occurs), then one is fairly safe in assuming that definite increase in the P-R interval is indicative of an underlying rheumatic fever.

The only other common acute disease that may produce similar heart block is *diphtheria*, but confusion between this and smouldering rheumatic fever rarely occurs. As an illustration the following experience may be cited:

**Case I.**—A young man, twenty-three years old, complained of palpitation of the heart of five days' duration. He had similar sensations for a short while five years ago with scarlet fever. He had otherwise been well, although in the past few weeks he had felt tired and had been given vitamins. The palpitation would come and go suddenly and lasted five to ten minutes.

Examination was entirely negative. The patient was a tall, thin young man. The blood pressure was 120/70. The heart was not enlarged; the rate was 103 and there were no murmurs. Temperature was 98.5.



Fig. 158 (Case I).—Note that conduction time is markedly delayed (P-R = 0.32 sec.). This is a common evidence of rheumatic fever.

At first I thought there was nothing wrong with the heart and could find no evidence of organic disease anywhere. After the electrocardiograms were examined, it was clear that the patient had a smouldering rheumatic fever with an active rheumatic myocarditis, for they showed a high degree of first degree heart block (Fig. 158). When this was known, on direct questioning the patient then admitted that he had lately noticed some mild aches in his knees and wrists. After several weeks' rest he made a complete recovery. The electrocardiograms in this case furnished the main data that were diagnostic.

**Cardiac Irregularities.**—The second group of patients in which electrocardiography can be valuable is when irregularities of the heart beat or disturbances in the cardiac mechanism are present. A well-trained clinician is able to diagnose most of these at the bedside, but even he finds some of the arrhythmias too difficult to decipher. The electrocardiogram gives a permanent undisputed record, however, which occasionally is needed.

From the practitioner's point of view there are certain irregularities that must be recognized accurately and others that are of less importance. A little greater attention to the bedside recognition of these arrhythmias, on the part of some physicians, is much needed, for accurate diagnosis is not difficult. It is not the purpose of this discussion to take up the question of diagnosis as it has been recently reviewed.<sup>1</sup> The general practitioner must realize that the correct interpretation

of an arrhythmia may be the first clue to a previously unrecognized diagnosis. Furthermore, a disturbance in the mechanism of the heart of itself may occasionally endanger the life of the patient and may yet be curable.

When ordinary isolated *extrasystoles* are detected, it is rarely necessary to determine whether they are auricular or ventricular in origin. This can be decided with certainty only by an electrocardiogram. There is too little difference in the clinical significance of the two types of extrasystoles to warrant taking a tracing. Rarely, however, it will be necessary to do so in order to help determine whether attacks of paroxysmal rapid heart action that occur in the same patient at other times are of auricular or ventricular origin. Inasmuch as such attacks may come and go abruptly and it may be impossible to make adequate examination of the spell itself, the finding of extra-auricular systoles during the interparoxysmal intervals would point more to paroxysms from the auricles and the finding of extraventricular systoles to paroxysms from the ventricles.

The determination of the *exact character of a paroxysm* of rapid heart action is often quite important. A gross irregularity is fairly typical of auricular fibrillation. A very rapid regular beat that comes and goes suddenly, and which is often stopped by vagal stimulation, is characteristic of paroxysmal auricular tachycardia. When the rapid heart rate is due to *auricular flutter* or to *ventricular tachycardia*, the diagnosis is not so simple. Although a trained cardiologist is often able to make these differentiations at the bedside, the average physician will require help and here the electrocardiogram can be very valuable. The inference from this is that, whenever an unusually rapid heart rate is found and is not readily identified, a tracing should be taken if possible. One can cite many instances where the determination of the exact disturbance in the mechanism of the heart beat was vital and even life saving.

The following experience illustrates the importance of *accurate diagnosis*:

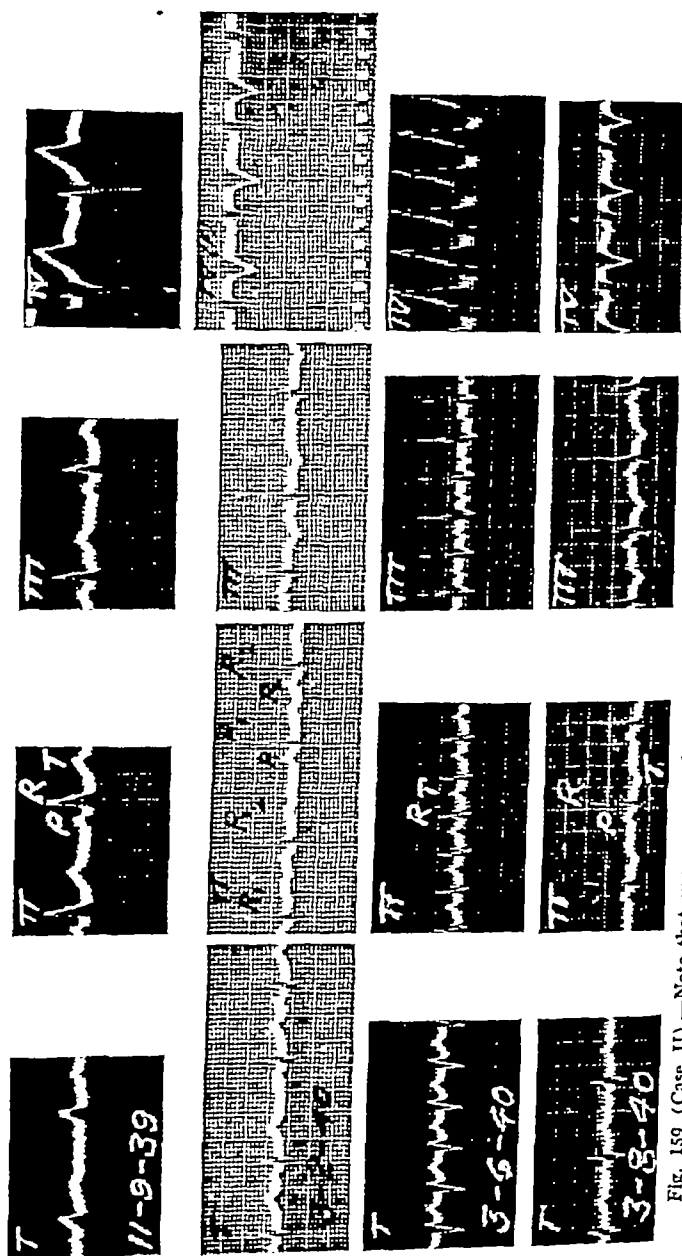


Fig. 159 (Case II).—Note that upper curves show intraventricular block (Q-R-S = 0.11 sec.). Second set shows disappearance of block and alternation of pacemaker. Every second beat is probably due to a slightly premature auricular impulse ( $P_4$ ). Third set shows a paroxysm of atrial tachycardia with a simultaneous intraventricular block (rate = 167). Lower curves show a return to normal rhythm.

Case II.—A man, sixty-five years old, who was known to have had previous coronary artery sclerosis and had showed bundle-branch block, developed phlebitis of the left leg. Shortly after this he had a pulmonary embolism to the left lung and was desperately ill. About three weeks after this, while he apparently was progressing satisfactorily, he suddenly developed a rapid regular heart with a rate around 170 to 180.

Electrocardiograms had been taken at various times and during the tachycardia (Fig. 159). While the heart was comparatively slow (90 to 100), they showed a normal rhythm. In most of the tracings there was constant bundle-branch block, although in some conduction was normal with sharp Q-R-S complexes. These curves at times also showed a peculiar disturbance in the auricles of the type that might be called an alternation of the pacemaker. The tracings during tachycardia could be interpreted in one of two ways: Either he had a paroxysm of auricular tachycardia with concomitant bundle-branch block or he had a ventricular tachycardia. The former should respond to carotid sinus pressure or other means of vagal stimulation and repeated attacks might be prevented by constant digitalization. The latter would not respond to any of the methods of vagal stimulation but should be controlled by quinidine. It is evident that treatment depended entirely on whether the attack was auricular or ventricular in origin.

Before seeing this patient during the attack of tachycardia I had advised trying carotid sinus pressure, but several attempts produced no effect. When I saw him the heart rate was about 170 and regular. Although he felt fairly comfortable the pulse was hardly perceptible. The blood pressure was barely made out at 80 mm. Only a few beats could be heard and then disappeared. The detection of an auricular disturbance in the electrocardiograms, when he was not in the attack (Fig. 159, second set of curves), and the constant regularity of the heart made me believe that the present disturbance was auricular tachycardia and should respond to vagal stimulation. Pressure on the right carotid sinus was ineffective, but stimulation of the left carotid sinus immediately brought the attack to an end and in a few seconds the heart rate was 85. The patient promptly improved and eventually recovered and became ambulatory.

On other occasions the situation is *reversed*: Tachycardia of ventricular and not of auricular origin is the cause of the emergency and this requires entirely different treatment. This arrhythmia is generally associated with grave coronary artery disease but occasionally occurs in an otherwise normal heart. When uncontrolled, the rapid heart rate may result in heart failure and death. The important practical point about *paroxysmal ventricular tachycardia* is that it cannot be helped by digitalis and, in fact, is made worse by this drug. It usually but not always responds to quinidine.



The following case illustrates the critical nature of the problem involved and the importance of electrocardiographic diagnosis:

**Case III.**—A woman, thirty-four years old, was seen in consultation with Dr. R. S. Starr of Hartford, January 17, 1936. For six months she had had several fainting spells of very short duration; otherwise she was well and carrying on normal activities. Twelve days before I saw her the present attack began. She noticed the sudden onset of palpitation which continued ever since. She continued her house work for several days and then she had grown increasingly weak and short of breath. During this time her heart was found

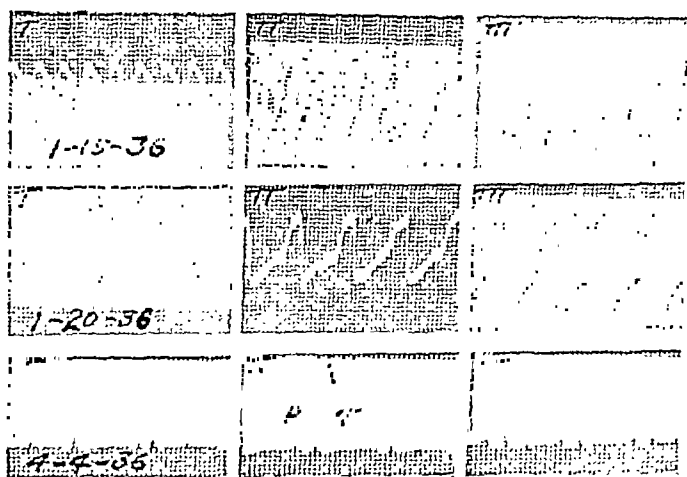


Fig. 160 (Case III).—Upper set shows paroxysmal ventricular tachycardia (rate = 247). Middle set shows the same mechanism—heart slowed to 122 on quinidine therapy. Lowest curves show return to normal rhythm.

to be extremely rapid, even as high as 260. Various medicines were tried without result. Carotid and ocular pressure were ineffective. Then 23 grains of digitalis were given in thirty hours without any slowing of the heart. Dr. Starr then was called, took an electrocardiogram and made the diagnosis of ventricular tachycardia. He advised quinidine therapy. During several days increasing amounts of quinidine were given orally, reaching the dose of 1.0 gm. (15 grains) at intervals of three hours. It was always noted that the ventricular rate would slow following large doses of quinidine from around 200 to about 140, but as the effect wore off, the original rapid rate returned.

When I saw the patient she was in a desperate state. She was semi-stuporous and in advanced congestive failure with free fluid in the pleural cavities, enlarged liver, and marked orthopnea. The blood pressure was diffi-

cult to obtain, but the reading was about 98/80. The heart rate was about 200 and regular. The electrocardiograms were typical of paroxysmal ventricular tachycardia (Fig. 160). The only drug that was known to break up this abnormal mechanism was quinidine. Inasmuch as partial effects had occurred following this drug, I advised increasing the dose further. During the next several days she received massive doses, from 110 to 150 grains a day. Finally, on January 25, I suggested that an hour after an oral dose of 35 grains of quinidine is given, when slowing effect on the ventricle was obtained,  $\frac{1}{50}$  grain of atropine be given subcutaneously. About two hours after this the attack came to an end and a normal rhythm was resumed. From then on she quickly recovered and has been essentially well ever since, showing no evidence of organic heart disease. This attack had lasted for eighteen days.

In an instance like this and in similar cases it would have been difficult if not impossible to carry out intelligent and effective treatment without the aid of electrocardiograms.

There are other types of "spells" in which electrocardiographic study is very important: Patients may have *faint feelings* or even attacks of *unconsciousness*. General physical examination may be entirely negative and one is apt to make diagnoses such as hysteria, petit mal, epilepsy, spasm of cerebral vessels, reflex or carotid sinus syncope, etc. It is well known that certain disturbances in the cardiac mechanism can produce syncope. A sudden marked slowing of the heart such as occurs in complete heart block or a sudden inception of a very rapid rate may be accompanied by a temporary state of *unconsciousness*. What is not sufficiently appreciated is that such cardiac upset may occur and yet show nothing abnormal in the heart between spells. We are accustomed to expect that a heart which is capable of developing an Adams-Stokes attack will show complete heart block or some disturbance in auriculo-ventricular conduction between attacks. This is by no means invariably true.

In cases of syncope, especially in patients over forty or fifty years of age, it becomes necessary, therefore, to make every effort to observe the attack and to study any possible disturbance of the heart during the momentary unconscious period, even when the heart at other times seems to be perfectly normal:

**Case IV.**—A woman, sixty years old, came to see me January 13, 1939, complaining of fainting attacks. During the previous two months she had three major spells when she fell unconscious for a moment or so and many minor ones when she would momentarily feel faint and dizzy. Otherwise she felt fairly well and could carry on normal activities. She had her eyes fitted for glasses without improvement and had been to a neighboring hospital for observation where the condition was thought to be hysterical or functional. When I saw her I learned that she had "rheumatism" at sixteen years of age. She also observed that her heart would thump after a spell. On examination she seemed quite well though apprehensive. The only abnormalities were a definite hypertension (195/95) and a late diastolic rumbling murmur at the

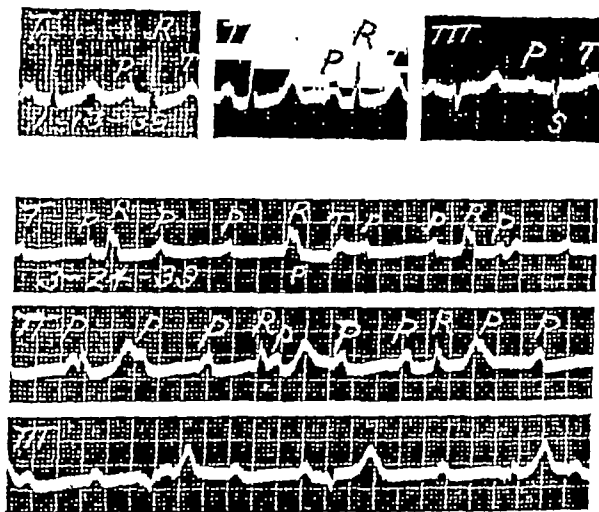


Fig. 161 (Case IV).—Upper set (1/13/39) shows normal rhythm. The "P" waves are prominent as occurs in mitral stenosis. Lower set (3/24/39) shows complete heart block.

apex clearly indicative of mitral stenosis. The carotid sinus reflexes were normal. The electrocardiograms were essentially normal, merely showing somewhat prominent auricular complexes (P waves) such as are seen in cases of mitral stenosis (Fig. 161).

I was at a loss for a satisfactory explanation of the attacks of syncope. It might be due to some cerebral vascular lesion, or, more likely, to some disturbance in the mechanism of the heart. The only possible way of making the diagnosis was to observe an attack. I told this to her family physician and urged him to make every effort to see her and examine the heart during an attack. One day, two months later, she began to have frequent attacks lasting about thirty to sixty seconds. When I was again called I eagerly stayed in the patient's home for two hours in order to observe the behavior

of the heart during a spell. The patient was kept wired to the electrocardiograph machine for an hour and I was finally rewarded for my efforts in catching a spell. The tracings showed that she was going in and out of complete heart block (Fig. 161) and that at times the heart actually stopped for some seconds. The diagnosis of Adams-Stokes disease was thereby established. At present she is free from attacks, but having had such a variety of medications it is difficult to tell which, if any, were responsible for the improvement.

One could continue at great length discussing peculiar arrhythmias in which electrocardiography proved valuable. From the practitioner's point of view, the general policy may be followed that whenever a cardiac irregularity is easily recognized and either readily controlled or causing no inconvenience to the patient, there is no need for further investigation. However, when it is puzzling or refractory to treatment, or if there is any possibility that it may be playing a significant rôle in the patient's symptomatology, its exact type should be ascertained by electrocardiography. Occasionally one will uncover conditions that were hardly expected, such as auricular flutter, and not infrequently the disturbances will be of the type that is amenable to treatment.

**Coronary Artery Disease.**—The third group of conditions in which electrocardiography may be very helpful is in coronary artery disease. It probably has its greatest diagnostic value in these cases. There are so many patients with angina pectoris, coronary thrombosis, or myocardial infarction that show nothing distinctly abnormal on ordinary physical examination that we often are dependent on laboratory methods to establish the correct diagnosis.

In making the diagnosis of either *angina pectoris* or *acute coronary thrombosis*, we all are aware of the fact that the history is all important. There really is no other diagnostic characteristic of angina apart from the history. When the typical story is obtained, it does not matter whether the physical, roentgenologic, or electrocardiographic examination is normal, we must make the diagnosis of angina unless we believe the patient is malingering. Often when the clinical diagnosis seems quite certain, electrocardiograms furnish confirmatory

data in showing evidence of myocardial involvement. There are many instances, however, where the history is atypical, and when the pain or distress in the chest might be due to gas, spondylitis, gallbladder disease, or a host of other conditions. It is in this group of patients that the electrocardiogram may show characteristic abnormalities of coronary artery disease. Just as has been mentioned above in regard to many other cardiac conditions, the physician does not need an electrocardiogram if the diagnosis of angina pectoris or coronary thrombosis is certain and well established. He should obtain a tracing, however, where the diagnosis is in doubt. It must be appreciated that finding a normal electrocardiogram by no means eliminates the diagnosis of either angina pectoris or coronary thrombosis. The information is valuable mainly when it is positive. Furthermore, a series of negative or normal tracings during the first ten days following an acute attack of some sort does point strongly against the possibility of an acute myocardial infarction.

Finally, the *distinction* between *myocardial infarction* and *coronary artery sclerosis* or narrowing must be clearly kept in mind. The electrocardiogram can only show evidence of a myocardial damage. This may be present without an acute coronary episode and, contrariwise, there may be slight or marked acute or chronic coronary disease without a myocardial infarct and in these cases the electrocardiograms may be unchanged.

It is clear from the above that electrocardiography may be very useful in appraising a heart that otherwise seems innocent. When the state of the heart muscle cannot be determined by the history or bedside methods, then a tracing may be very informing. One should, therefore, be ready to use electrocardiography rather freely in patients suspected of coronary artery sclerosis, especially in males over forty years of age with atypical symptoms.

It is a not infrequent experience, even for expert cardiologists, suddenly to find *pathognomonic evidence* of grave coronary artery disease in patients they were ready to regard

as having a *normal* heart. The following cases will serve as examples:

**Case V.**—A man, sixty-four years of age, came to my office with the following story: He regarded himself as well except for a slight cough and slight shortness of breath on climbing stairs for ten years. He had been treated for chronic bronchitis and slight emphysema for many years but was able to carry on all his usual duties. He never had any pain in the chest and was able to walk freely without distress. About a week before, when seeing his physician, a few extrasystoles were heard. About this time he had a peculiar mild discomfort in the precordial region that he had difficulty in describing. It did not concern him much as he was able to carry on his work. His physician saw him for several days, and found no fever or any other changes from his previous state.



Fig. 162 (Case V).—Note Q-R-S complexes are rather small in first three leads. There is a prominent  $Q_2$  and  $Q_3$ . The initial upward ventricular deflection is absent in Lead 4 and  $T_4$  is rounded and dipped. These curves are indicative of myocardial infarction.

On my examination there was nothing remarkable to detect except for slight emphysema which somewhat obscured the heart borders and the intensity of the heart sounds. There were a few scattered expiratory bronchial squeaks. The blood pressure was 135/85, where it had always been. There was no enlargement of the heart and no murmurs were heard. Inasmuch as he then looked and felt well (the mild discomfort had disappeared), I believed that his heart was sound. The patient was told that he had nothing to fear concerning his heart. An hour or so later, when the electrocardiogram that had been taken was developed, I found to my great surprise that the curves indicated an anterior myocardial infarction (Fig. 162). I had to revise the entire diagnosis and treatment of this case as a direct result of the electrocardiographic data.

There are a variety of abnormalities, particularly in the *ventricular complex*, that may indirectly help in the diagnosis of coronary artery disease. The most common finding is an abnormal form or inversion of the T wave. Frequently, bundle-branch block or intraventricular block is found. Occasionally some degree of a-v block is present. Some alterations in the electrocardiograms result from causes other than pri-

mary heart disease, such as digitalis administration, pulmonary embolism, etc. The physician must be aware of this and also appreciate that, even when abnormal electrocardiograms are found, they may be the result of some old and quiescent lesion and have nothing to do with the presenting complaint. The main deduction that can be made is that certain alterations in the tracings do indicate heart muscle disease, old or recent, and when the question arises whether a heart is perfectly normal or whether there is coronary disease, the finding of distinctly abnormal electrocardiograms may decide the issue.

**Case VI.**—A physician, forty-two years of age, came to my office complaining of faint feelings. He was well up to three weeks before. On a particularly hot day he suddenly felt faint. He was kept in bed several days. He then tried to return to work but kept having peculiar spells. It felt as if something stopped for an instant and his heart skipped. With this there was tingling in the legs and left hand, general weakness and belching of gas. There was absolutely no pain with this. His symptoms were not related to effort or to meals. The spells recurred daily and he otherwise felt well. During these three weeks there was no fever, leukocytosis, increase in sedimentation rate, or change in blood pressure.



Fig. 163 (Case VI).—Note the slight rounding and dipping of T. Although this is not marked, it is very suggestive of coronary artery sclerosis.

On examination I found only a faint systolic murmur and a definitely sensitive left carotid sinus. Pressure in this region reproduced the faint feelings. I thought there was little, if anything, wrong with the heart until I saw the electrocardiogram. In fact, I was ready to believe that he may have had some benign extrasystoles, a sensitive carotid sinus but otherwise was well. The finding of distinctly abnormal ventricular complexes (Fig. 163) led to the diagnosis of coronary artery sclerosis. One might regard this as a rare instance of angina sine dolore.

The following is another instance in which electrocardiography furnished valuable information:

**Case VII.**—A dentist, fifty-two years old, complained of a mild, dull constant feeling in the precordium. He had had this feeling off and on for ten years. He thought it might be related to the position he assumed in his

work. It was not related to effort and he could walk briskly without any added discomfort. Examination was entirely negative. The heart was not enlarged, the sounds were normal, and there were no murmurs. The blood pressure was 126/78.

At first I thought he had no disease of the heart and that the mild ache in the left breast was of the type frequently found unassociated with heart disease. The electrocardiograms (Fig. 164), however, were typical of right

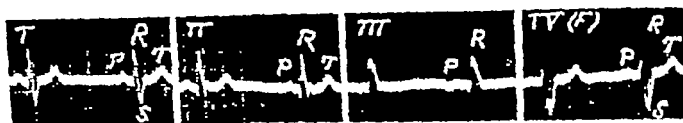


Fig. 164 (Case VII).—Note the spread Q-R-S waves (0.11 sec.). They are indicative of right bundle-branch block.

bundle-branch block. It then became clear that he probably had coronary artery sclerosis as the most likely cause of such abnormal tracings. I did think that the precordial ache was not anginal in type nor due to the heart. During the past four years, since he was first seen, he has been very well and active, carrying on a busy practice in dentistry and playing eighteen to thirty-six holes of golf on frequent occasions. In this instance the electrocardiograms revealed evidence of myocardial disease that otherwise could hardly be suspected.

There are numerous instances where *bundle-branch block* or *intracardiac block* are found and there is very little other evidence to incriminate the heart. The following is such an example:

Case VIII.—A woman, fifty-seven years old, complained of "stopping of the heart." For many years she noticed that her heart would suddenly jump

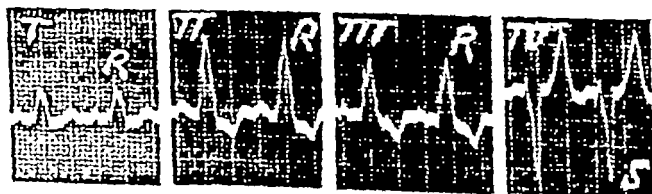


Fig. 165 (Case VIII).—Note the markedly spread Q-R-S waves (0.12 sec.). Such curves indicate intraventricular block or bundle-branch block.

or skip. This would come mainly while she was at rest and in bed. She had no dyspnea or pain in the chest and was able to do her work or walk normally. Examination was entirely normal. The heart was not enlarged and showed



no murmurs or irregularities. The blood pressure was 122/78 and had never been high. The fact that she did not have hypertension made me feel all the more certain that she had no significant coronary artery disease, because women of her age who have not had hypertension rarely have much coronary sclerosis. The electrocardiograms (Fig. 165), however, showed intracardiac block for which there is no more likely explanation than coronary sclerosis. I do believe that the heart had not yet shown any symptomatic evidence of disability.

**Miscellaneous Conditions in which Electrocardiograms Are Helpful.**—The final group of cases in which the electrocardiograms may indirectly be helpful is a heterogeneous one. They are not instances in which the heart tracings are of primary importance, though they may afford supportive evidence for or against certain diagnoses.

A patient may be suspected of having *myxedema*. If the electrocardiograms show perfectly normal complexes with large upward T waves it is unlikely that well-marked myxedema is present. On the other hand, if the ventricular complexes are all low and the T waves are flat, such changes would support the diagnosis of myxedema. Likewise, a rare condition like *hypocalcemia* from hypoparathyroidism might be suspected on finding a markedly lengthened Q-T interval. Occasionally in cases of *pulmonary embolism* the electrocardiogram may be helpful in diagnosis. Such and other experiences are much less important to the general practitioner than the above three conditions that have already been discussed, because they are comparatively rare. Suffice it to mention that occasionally electrocardiography may throw light on conditions that apparently are unrelated to the heart.

**Limitations in Interpretation of Electrocardiograms.**—Before bringing this discussion to a close, I must emphasize a word of caution against the *overenthusiastic* use of electrocardiography. The electrocardiograph machine itself has become so simple and comparatively inexpensive that there are thousands of them in use. Many inadequately trained physicians have assumed the responsibility of interpreting the tracings and the result is that there is a danger of prostituting the entire work. There are many laymen and still too many

physicians who take the view that an electrocardiogram can decide whether there is or is not heart disease.

Too often tracings are *misinterpreted*. It is amazing what serious errors are made by trying to read too much into electrocardiograms. I have frequently had electrocardiograms sent to me for interpretation when the diagnosis of coronary artery disease had been made entirely on changes in the ventricular complex. In many such instances technical errors accounted for the misinterpretation of the curves. In some the electrodes were wrongly applied. In others the leads were incorrectly numbered. At times the tracings were pasted on incorrectly, so that the end of the curve appeared at the beginning or the top and bottom were reversed. I have even been asked to interpret an electrocardiogram where it was quite clear that curves of two patients had been taken simultaneously on the same film. Coarse tremors and intricate artefacts have been misinterpreted as ventricular fibrillation. In one such case that even appeared in a reputable medical journal,<sup>2</sup> one could trace the normal regular heart beats throughout the otherwise bizarre electrocardiogram. The muscular movements of the infant and possible jarring of the lead wires had produced numerous deflections in the electrocardiogram that misled the author to regard it as ventricular fibrillation.

Apart from the above technical errors, one must be careful in observing whether the tracing is *well standardized*. If there is overshooting of the string or if the skin resistance is high enough to cause a sluggish deflection time, the ventricular complex is necessarily distorted. The height of the waves may be too great or too small and what is more important, the Q-R-S complex may become falsely lengthened in its duration. One can readily see that grave errors in diagnosis may result purely from errors in technic.

Finally, the clinical interpretation of electrocardiograms that are properly taken is no simple matter. There has been too great a desire to make extensive pathologic diagnoses from *minor alterations* in the tracings. Notching of the Q-R-S

waves or slight flattening of the T waves may be abnormal and yet of no clinical importance in a given case. Even more outspoken aberrations from the normal configurations of the electrocardiogram may be present and yet be unaccompanied by either angina pectoris or myocardial weakness. I have seen instances of right bundle-branch block for fifteen to twenty years in individuals who have been able to carry on an active life. One such young man at present shows no signs or symptoms of heart disease and yet has had such curves for nineteen years.

The main *misuse* to which electrocardiography is being put at present is in *prognosis*. There is no doubt of its great diagnostic value. Numerous conditions can now be recognized by electrocardiography that were entirely beyond the reach of the greatest clinicians of the past. The difficulty is that, once a diagnosis has been established, changes in the electrocardiogram add very little to the prognosis. From then on experienced clinical judgment may be far superior to the prognostic opinions that are offered by the so-called electrocardiographic expert. During the progress of a definite acute coronary thrombosis the curves may show very little abnormality or may be returning to a more normal form while the patient is obviously growing worse or dying. On the other hand, marked electrocardiographic changes may be going on in a case that runs a mild course and does very well. There is no great advantage in taking frequent tracings in a known case of acute coronary thrombosis except if something happens that makes the physician think that a fresh involvement or extension has occurred. Even then the clinical course is likely to be a more important guide of the progress of events.

Furthermore, little of importance is learned from tracings taken every week or month after recovery from an acute coronary thrombosis. Patients may do poorly who show very little in the electrocardiograms or who show no further changes and they may do very well having been left with such striking abnormalities as bundle-branch block, marked reduction in

the amplitude of the Q-R-S complex or permanently inverted T waves.

Although there are statistical studies indicating that in conditions like bundle-branch block or inverted T waves in Lead I the average length of life is about one to two years, it requires clinical judgment to apply such data to individual cases. There are frequent instances in which patients with such severe abnormalities carry on satisfactorily for many years. I recall seeing a woman, sixty-six years old, with hypertension who was regarded as having grave heart disease because of certain symptoms she had and she was given a prognosis of six to twelve months mainly because she had an inverted T wave in Lead I. She had been studied in a very large and active clinic. She complained of some dyspnea and cough. There were râles at the left base of the lung. Blood pressure was 195/110 and the electrocardiograms showed a high degree of left axis deviation with an inversion of  $T_1$ . The interpretation I made was quite different from the ominous one she had previously been given. A cardiac with pulmonary congestion is much more apt to have râles at the right rather than the left base. This finding was, therefore, looked upon as due to bronchitis or bronchiectasis. There was no other clinical evidence of cardiac failure except for the shortness of breath. This many elderly obese hypertensives have even without failure of the heart. She was told to stop all cardiac medication, given a simple sedative and encouraged to carry on. After ten years of a useful life, during which time she always showed râles at the left base of the lungs and not at the right, she began to have weakening of the heart and now takes digitalis for dyspnea. The electrocardiograms have shown about the same type of inverted  $T_1$  during these past ten years.

I have seen similar patients with left axis deviation and inverted  $T_1$  carry on for even twenty years without evidence of heart failure. Mention has already been made of cases of bundle-branch block carrying on satisfactorily for many years.

There are even instances in which patients have shown electrocardiograms of extremely low amplitude after coronary thrombosis for a great many years, during which time they were in good condition.

The main conclusion from all this is that prognosis in such cases could have been judged more accurately from *clinical* than from electrocardiographic data.

**Summary and Conclusions.**—There are three main groups of cases in which the general practitioner may find electrocardiography helpful: The first is during an atypical infection, where disturbances in auriculoventricular conduction or alterations in the ventricular complex may aid in establishing a diagnosis of acute rheumatic fever. The second is in deciphering arrhythmias that are otherwise difficult or impossible to diagnose. The third is in the diagnosis of angina pectoris or any form of acute or chronic coronary artery disease.

There are certain conditions that can be diagnosed by electrocardiography that cannot possibly be detected by any other means. Although its diagnostic value is great, its prognostic value is limited. In estimating prognosis, clinical judgment is superior to relying on the statistical averages that have been published in relation to electrocardiographic changes such as bundle-branch block and inversion of the T waves. Once a diagnosis has been established, little is gained by taking frequent electrocardiograms unless a new condition has developed.

There are errors in technic in electrocardiographic work that lead to grave diagnostic mistakes. There is also a tendency to attach too much clinical significance to minor abnormalities in electrocardiograms. Because of the increasingly widespread use of this method of study by inadequately trained physicians, there is a danger that the entire subject will be prostituted and fall into disrepute.

The finding of abnormal electrocardiograms does not necessarily mean that the heart is the cause of the patient's primary complaints. It still has to be correlated with all other clinical features, for the patient may be actually suffering from

a pulmonary embolism, a ruptured peptic ulcer, or one of a great variety of noncardiac conditions and yet show abnormal tracings.

Electrocardiography does not enable the physician to eliminate the possibility of organic heart disease, but it does aid in treating some patients successfully who otherwise would succumb.

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VOL. 24—85



## CLINIC OF DRS. EUGENE C. EPPINGER AND C. SIDNEY BURWELL

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### CURABLE HEART DISEASE

#### INTRODUCTION

TREATMENT in heart disease is most frequently concerned not with cure but with the postponement or temporary relief of disability. Such management is often successful in that it enables patients to live long and productive lives, but it does not often eliminate the underlying abnormality. In recent years, however, advance in knowledge has made it possible to bring about the *cure* of heart disease in certain cases. The word "cure" is used to indicate: (1) the inactivation or abolition of a disease process while its effects are still reversible, and (2) the repair of a disabling mechanical defect left by some injury or disease no longer active. The object of this clinic is to present a discussion of the diagnosis and treatment of several varieties of heart disease which may be called "curable," and to consider as examples cases illustrating some of the problems and achievements of such diagnosis and treatment.

Patients with curable heart disease may be considered in three groups as follows: (1) A group of patients in whom the cardiac disability is a result of severe *mechanical overload* of the heart. The lesions or defects leading to such overload include patent ductus arteriosus, arteriovenous fistula, thyrotoxicosis and possibly anemia. (2) A group of patients in whom the cardiac disability results from a *mechanical obstruction* to the entrance of blood into the heart. Such obstruction



occurs in the various forms of cardiac tamponade, notably those due to constrictive pericarditis, suppurative pericarditis and acute hemopericardium. (3) A group of patients in whom the cardiac disability is due not to a gross mechanical abnormality, but to a *dysfunction of the cardiac muscle*. This group includes patients who suffer from beriberi heart and the so-called myxedema heart.

#### GROUP I. MECHANICAL OVERLOAD

**Patent Ductus Arteriosus.**—Patency of the ductus arteriosus is the persistence of a communication between the aorta and pulmonary artery, which is necessary during fetal life, but which normally closes at, or soon after birth. Recently Gross and Hubbard<sup>1</sup> have described the successful closure of this abnormal channel by ligation.

**Case I.**—This patient (F. S.), was observed first as a girl of six years. She was known to have had a loud murmur in the cardiac area since the age of three years. She had always been underweight, but had been able to lead a fairly active life with some limitation by dyspnea on moderate exertion.

On physical examination the patient was found to be pale, thin and definitely underdeveloped for her age, her weight being 18.3 kg. and her height 117.5 cm. The left chest bulged forward and there was a widespread cardiac pulsation which lifted the whole chest as far out as the nipple line. A rough thrill was felt, maximal in the second left interspace and most intense in systole. In this same area there was a loud continuous murmur. The blood pressure was 98/40, and the vital capacity 1000 cc. Studies of the blood and urine were normal. The electrocardiogram was normal. Roentgenograms and fluoroscopic examination of the heart showed slight cardiac enlargement to the left. The transverse diameter of the heart was 9.8 cm., the internal diameter of the thorax 18.6 cm. There was a bulge in the region of the pulmonary artery and vigorous pulsation was observed in both the pulmonary artery and its branches.

In November, 1938, the patent ductus was ligated by Dr. R. E. Gross.<sup>2</sup> On exposure of the heart its action was observed to be extremely forceful. A thrill could be palpated over the entire organ, and particularly over the pulmonary artery. Occlusion of the ductus immediately brought about a most striking change. The cardiac action became quiet and slow, the thrill disappeared and the diastolic pressure rose from 50 to 80 mm. of mercury.

This patient has been followed at intervals for fifteen months after operation. The cardiac murmur has disappeared

except for a very soft systolic blow in the pulmonary area. The blood pressure remains at about 92 systolic and 70 mm. of mercury diastolic. She has gained 5 kg. in weight and grown 8.6 cm. in this period. A roentgenogram of the heart at this time shows a decrease in the transverse diameter of 1 cm., with the diameter of the thorax remaining essentially the same. The pulmonary artery is definitely less prominent and pulsations in its branches are not evident. Subjectively, it is noted that the child has become actively interested in games and is in no way limited in her capacity to enjoy them.

*Diagnosis of Patent Ductus Arteriosus.*—The recognition of these cases is dependent primarily upon the presence of the characteristic *loud continuous murmur* in the pulmonary area. Also, as Bohn<sup>3</sup> pointed out, the *level of the diastolic pressure* may be low and the pulse *collapsing* or *quick* in character. The presence or absence of this sign appears to be related to the size of the ductus and consequently to the amount of regurgitation from the aorta into the pulmonary artery. This phenomenon may be exaggerated by excitement or exercise. Retardation in physical development is associated with many congenital cardiac abnormalities, of which patent ductus is only one.

Confirmatory information may be gained from the *roentgenologic examination* of the heart. The left ventricle may be moderately enlarged and its excursions greater than normal. The pulmonary artery is unusually prominent and, when viewed on the fluoroscopic screen, a marked systolic pulsation may be seen. In addition, its branches are frequently more prominent than normal and occasionally these may be seen to pulsate. A striking but little emphasized finding is that of *pulmonary congestion*.

*Pathologic Physiology.*—Limitation of activity, the subsequent development of congestive heart failure, and the physical and roentgenologic signs of this disease are dependent upon the *abnormal flow of blood* through the heart and lungs. Opportunity to study this problem was provided by Dr. Gross' operation for ligation.<sup>4</sup> By comparing the oxygen content of

the blood in the aorta and that in the pulmonary artery before and after ligation of the ductus, information concerning this abnormal flow of blood has been obtained. Since there is a higher mean blood pressure in the aorta than in the pulmonary artery, blood should flow from the aorta into the pulmonary vessel in both phases of the cardiac cycle. Thus, the volume of blood flowing through the pulmonary circuit should be increased, with a consequent and corresponding increase in the output of the left ventricle. That such is the case has been demonstrated by studies made upon six patients at the time of operation.

From 45 to 75 per cent of the blood pumped out by the left ventricle was returned to the lungs through the ductus. As a result of this addition of blood to the pulmonary circulation, the output of the left ventricle was found to be two to four times that of the right. In the light of these observations, it can be readily understood why a loud continuous murmur, a low diastolic pressure, dilatation and even pulsation of the pulmonary artery and its branches, and enlargement of the left ventricle are found. The greatly increased burden upon the left ventricle supplies an adequate reason for eventual congestive heart failure.

*Indications for Operation.*—The cases selected for operation should come from the group seriously disabled by limitation of their cardiac reserve or from those whose retarded growth indicates a large leak. The presence of other congenital cardiac anomalies may be suggested as a deterrent to operation. For practical purposes it may be taken that *if cyanosis is not present*, the additional lesions, if they do exist, do not contraindicate operation.

A serious *complication* of this congenital abnormality is subacute bacterial endocarditis; whether or not ligation will decrease the likelihood of this complication can only be determined by a long period of observation upon patients treated surgically.

*Arteriovenous Fistula.*—The preceding case was an instance of leak or shunt from the aorta to the pulmonary artery,

leading to wasted effort on the part of the heart, cardiac overwork, and eventually cardiac failure. A similar chain of events may occur when the leak is from artery to veins, as it is in arteriovenous fistula. Such a fistula may occur as a congenital vascular anomaly, or following a wound, usually of the penetrating variety. The leak causes a loss of blood from the arterial to the venous system without passage through capillaries. If the volume per minute shunted in this way is large, it may be necessary for the heart to increase its output and thus its work. The increase in work brought about by a large fistula (especially one near the heart) may be great enough to limit the cardiac reserve and lead eventually to congestive failure.

*Diagnosis.*—The diagnosis of arteriovenous fistula is usually made by a characteristic combination of physical signs. The enlargement of arteries and veins adjacent to the fistula may give a swelling or *localized tumor*. Near the leak is to be felt a *purring thrill*, usually continuous and with a systolic accentuation; this vibration is heard also as a loud murmur, widely conducted. The *pulse pressure* is increased, chiefly by a fall in the diastolic level. The *basal heart rate* is elevated. If the fistula is single and accessible, the flow through it may be temporarily abolished by compression; when this is sudden there is often a prompt slowing of the pulse. The dilated veins near the fistula may be observed to pulsate and blood drawn from them often has an oxygen saturation approaching that of arterial blood. The pressure in these veins is elevated above that in veins distant from the fistula. In many cases *the heart itself is enlarged*. That this enlargement is chiefly dilatation is shown by the reduction in heart size which commonly follows elimination of the fistula by operation.

*Treatment.*—When limitation of cardiac reserve or congestive failure occurs as a result of an arteriovenous fistula, the outlook for relief is often good provided the abnormal connection is accessible to operative closure. Porter<sup>5</sup> has described a case in which the heart size (by roentgenogram) was

reduced from 21.5 to 15.2 cm., after the fistula, a traumatic one, had been present for years. It appears, then, that cardiac failure associated with a large arteriovenous fistula is a type of heart disease which can be prevented or even cured by appropriate therapy.

A particularly exciting variety of curative therapy was described by Hamman and Rienhoff.<sup>6</sup> Their patient had the signs of arteriovenous fistula plus the signs of infection and embolism often observed in connection with subacute endocarditis. In the absence of any endocardial lesion as a site for such an infection, they shrewdly suspected that it was localized in the arteriovenous aneurysm. Operation disclosed the presence of a vegetation in the lumen between the two vessels. Removal of the fistula not only cured the disorder of the circulation, but eliminated the infection.

Present methods of treatment of *subacute bacterial endocarditis* are not sufficiently effective to have much influence on the course of the disease in most cases; however, current advances in chemotherapy make one hopeful that means will be found for the effective treatment of subacute bacterial endocarditis by chemical agents. There are already on record cases which suggest that the course of gonococcal endocarditis may be favorably influenced by sulfanilamide.

**Thyrotoxicosis with Cardiac Disability.**—Thyrotoxicosis is a form of thyroid disorder in which there are important changes in the work required of the heart:

**Case II.**—The patient (N. D.), a fifty-one-year-old painter, entered the hospital because of dyspnea, edema and palpitation of three months' duration. Until the onset of his illness he had always enjoyed excellent health. One year prior to his entry he developed a troublesome, dry, hacking cough, but there were no other symptoms until about three months before entry when he began to notice shortness of breath while walking on the street or when climbing stairs. Shortly thereafter his ankles swelled, this being more marked toward the end of the day. These symptoms gradually increased in severity and, six weeks before coming to the hospital, palpitation became evident and disturbing. His last month at home was one of marked discomfort because of the edema, pounding of his heart, and dyspnea so severe as to keep him from sleeping.

Physical examination showed a well-developed and nourished man propped

up in bed and breathing with difficulty. His facial expression was anxious and his color ruddy. The right eye was slightly more prominent than the left, but there was no lid lag or inability to converge. The thyroid gland was not enlarged, and the veins in the neck were moderately distended. The heart was enlarged to the left and its rhythm grossly irregular, with an apex rate of 130 per minute and a pulse deficit of 30. A soft systolic murmur was heard at the apex and the first sound was loud and snapping in quality. Slowing of the heart rate followed rest and digitalis. At this time several observers noted a diastolic rumble at the apex. The arterial blood pressure was 200 systolic and 100 diastolic. Examination of the lungs showed numerous râles posteriorly. The liver was enlarged and tender and there was marked edema below the knees.

Studies of the blood and urine were normal except for a moderate amount of albuminuria, which soon disappeared. The circulation time was sixteen seconds (sodium cyanide), the vital capacity 1900 cc., the blood cholesterol 202 mg. per cent, and the phenolsulfonphthalein excretion 90 per cent in two hours and ten minutes. Roentgenograms of the heart showed slight cardiac enlargement, but no prominence of the left auricle or intracardiac calcification. Electrocardiograms showed auricular fibrillation and slight left ventricular preponderance.

It was the consensus that this patient had hypertensive heart disease, though some observers contended that there was definite mitral stenosis. Accordingly, he was thoroughly digitalized and observed for a period of ten days. Contrary to the usual experience in early failure in hypertensive cases, this patient improved only moderately, and more particularly it was noted that, while the pulse deficit disappeared, the heart rate continued to be between 80 and 90 per minute. It was also observed that, in spite of absolute bed rest, the patient perspired almost constantly. The systolic blood pressure, as would be expected, fell to about 170 mm. of mercury, but the diastolic pressure was consistently at a level of 64 to 70 mm. At this time, it was suggested (by Dr. S. A. Levine) that the congestive heart failure was in the main due to hyperthyroidism. A determination of the basal metabolic rate gave a level of  $+47$  per cent, and on repeated determinations it averaged  $+34$  per cent. It was considered that the dyspnea was not of sufficient severity to increase the metabolic rate appreciably. After seven days of iodine therapy, there was a remarkable improvement in the patient's symptoms,

and the pulse rate fell to a level of 60 to 70 beats per minute. However, doubt concerning the presence of hyperthyroidism persisted in the minds of many and iodine was discontinued. The metabolic rate promptly rose to  $+48$  per cent and the pulse rate to 90 beats per minute, other conditions remaining the same. Iodine was again given, with a fall in the basal metabolic rate to  $+8$  per cent. A subtotal thyroidectomy was performed and a small but diffusely hyperplastic gland was found. Shortly after operation the cardiac rhythm became normal without the use of quinidine, the vital capacity increased to 3200 cc., and the evidences of congestive failure completely disappeared. The blood pressure remained at 180 systolic and 90 diastolic.

This patient has now been followed for five years and, during this period, he has been able to lead a normal, active life. Recently, however, the blood pressure has risen (to 210/120), and the symptoms of congestive heart failure have reappeared.

This case illustrates the rôle that hyperthyroidism may play in precipitating the onset of heart failure. As would be expected, it most often produces this effect in patients whose cardiac reserve is already reduced by degenerative or valvular disease. So far as we know, hyperthyroidism exerts its deleterious effect by increasing the work demanded of the heart. This burden is not discontinuous, like that of physical exertion, but is present both day and night. The burden of thyrotoxicosis which leads to heart failure may also act to produce seizures of angina pectoris in patients whose coronary blood supply is limited. In these cases, as in those of congestive failure, the relief afforded by subtotal thyroidectomy is frequently dramatic.

*Diagnosis of Thyrotoxicosis.*—Thyrotoxicosis manifesting itself as it did in this patient is often quite properly termed "masked hyperthyroidism,"<sup>7, 8</sup> since the usual evidences of its presence are so obscured by the symptoms and signs of heart failure. However, there are certain distinguishing characteristics which suggest hyperthyroidism even under these circum-

stances and which may lead to its recognition. Most of the patients will be found to be individuals over forty years of age. The thyroid may not be demonstrably enlarged. When enlargement is present it will usually be of nodular type rather than diffuse hyperplasia. *Nervousness* persisting after prolonged rest is a notable symptom. The presence of constant and excessive *sweating* is a helpful clue. Another suggestive sign is a *wide pulse pressure* in the absence of aortic insufficiency. *Auricular fibrillation*, particularly of the paroxysmal type, is frequent. The effect of digitalis upon this rhythm when it is associated with hyperthyroidism is peculiar. In most instances of congestive failure with auricular fibrillation (not due to thyrotoxicosis), digitalis in adequate amounts will slow the ventricular rate to a level of 60 to 70 beats per minute. However, in cases associated with thyrotoxicosis it is often noted that, in spite of doses of the drug large enough to produce intoxication, the ventricular rate does not slow below 80 to 90. Moreover, this type of therapy, as well as other accepted measures for the treatment of heart failure, fails to bring about the expected degree of improvement.

It is not uncommon to find that a diagnosis of mitral stenosis has been made in these cases. The heart is hyperactive, the first sound loud and often reduplicated, and at times the marked vibration associated with the first sound may simulate a thrill. With advanced left heart failure it is the usual experience to find the *circulation time* prolonged. In the case reported, it was sixteen seconds, an essentially normal figure in spite of a vital capacity of 1900 cc. A normal circulation time in a patient with heart failure should therefore raise the question of the presence of hyperthyroidism. Likewise, a phenolsulfonphthalein excretion of 90 per cent is higher than the usual finding in heart failure, and also suggests thyroid disease as a factor.

Finally, the *basal metabolic rate* may bring conclusive evidence. It is well known that the metabolic rate may be elevated by congestive heart failure per se, principally because of dyspnea and the muscular effort associated with it. How-



ever, if the rate remains consistently elevated after appropriate therapy has diminished the symptoms of heart failure, then this elevation should suggest hyperthyroidism. Further, almost indisputable evidence may be gained in doubtful cases by a therapeutic test with iodine.

*Treatment.*—The response to iodine treatment alone may be so successful that operation will be refused. In spite of this apparent cure with iodine alone, operation must be urged since under continuous iodine therapy most of these patients will have a recurrence of the hyperthyroidism. Happily, the operative mortality is low in spite of cardiac failure. Local or ether anesthesia may be used with good results.

The recognition of this important precipitating factor in congestive heart failure may save the patient many years of debilitating symptoms and, not infrequently, it may be a life-saving measure. Since so much is to be gained by the discovery of hyperthyroidism, it is important to consider it in any patient with heart failure, and particularly in those whose response to the usual forms of therapy is unsatisfactory.

**Anemia with Cardiac Disability.**—It is probable that the heart failure which occasionally occurs as the result of severe anemia is influenced by both mechanical and chemical factors. The work of the heart is measurably increased when the hemoglobin falls below 50 to 60 per cent, and at lower levels the increase may be very great.

Under such conditions of overwork the need of the heart for oxygen must be increased, and of course in severe anemia the facilities for the transportation of oxygen are greatly impaired. Whatever the mechanism, the fact is that very severe anemia may lead to cardiac dilatation and congestive failure which, in time, may be relieved, apparently permanently, by the restoration of the hemoglobin to normal levels.

In certain people in middle or old age, the occurrence of angina pectoris is closely related to the level of the hemoglobin. This form of angina may be relieved by the simple expedient of abolishing the anemia.

## GROUP II. CARDIAC TAMPONADE

**Chronic Constrictive Pericarditis.**—This condition is defined as a thickening of the pericardium which interferes with the filling of the heart:

**Case III.**—The patient (G. M.) is a young man who had been in good health until 1931, when he developed a pleural effusion accompanied by dyspnea and fever. A year later he had swelling of the abdomen, also with fever, and upon entering the Peter Bent Brigham Hospital he was found to have ascites. The ascitic fluid contained tubercle bacilli. He also exhibited a large heart shadow of "water-bottle shape," a beat of small amplitude, distended neck veins and cyanosis of the nail beds. Diagnoses of tuberculous peritonitis and pericarditis were made and he was sent to a sanatorium. Here he improved to some degree and, after two years, was discharged as having an inactive infection. At this time he was free from dyspnea and other discomfort while at rest, but even mild exertion, such as walking on the level, produced respiratory distress. As a result of this limitation he was unable to do the work upon which his livelihood depended.

About a year after his discharge from the sanatorium he was seen again in the Peter Bent Brigham Hospital. During this year his situation had remained essentially unchanged. When examined at this time (1935) his face had a suffused look, the nails were faintly cyanotic, the hands and feet were cold. The neck veins were distended and firm to the touch. The cardiac dulness was not increased, and did not shift with change of position. The basal heart rate was  $\pm 80$ , the rhythm was regular, and no murmurs were heard. The lungs showed the x-ray signs of apical fibrosis, but no moist râles were heard. The liver edge extended 3 or 4 cm. below the rib margin. The arterial pressure was 108 systolic and 90 diastolic and fluctuated with respiration, falling about 10 mm. during inspiration (pulsus paradoxus). The venous pressure was 175 mm. of water, the arm-to-tongue time thirty seconds. Under the fluoroscope the excursion of the heart appeared diminished, especially on the right.

This history and these observations were considered indicative of constrictive pericarditis. Because this was believed to be of only moderate severity there was some doubt about the necessity of operation. The patient was seen and studied repeatedly during the next two years. Various therapeutic regimens were tried but, at the end of the period, the signs and the limitations to activity were not greatly changed, and the venous pressure was a little higher.

In February, 1938, Dr. Elliott C. Cutler undertook a decortication of the heart. The heart, particularly in the region

of the right ventricle, was sheathed in fibrous tissue which seemed to limit the movements of the muscle beneath it. When the thick portion of this epicardial scar was shaved away the ventricle bulged forward and its excursion visibly increased. During the dissection a pocket of cheesy material was opened.

Within a few days of the operation the suffusion of the face disappeared, the cyanosis of the nail beds was replaced by a normal pink color, and the hands were no longer cold and clammy. The venous pressure fluctuated somewhat over a period of weeks, then gradually returned to normal. On increasing activity the patient gained strength and, in a few months, his capacity for work had returned to that of a healthy man.

*Diagnosis of Constrictive Pericarditis.*—This condition is a form of heart disease which may be cured. It is usually a sequel to tuberculous pericarditis, occasionally it is due to the *Staphylococcus aureus*, and apparently it is not produced as a result of rheumatic pericardial disease. Because it may be cured (particularly if the causative tuberculosis be not too progressive), it is of vital importance to recognize it. It is to be thought of when one encounters *peripheral congestion* or *ascites* in the absence of hypertension or obvious valvular disease, especially if the heart is normal in size or only slightly enlarged. Sometimes, as in this case, the development of obstruction as a sequel to acute pericarditis may be observed. More often, the case comes under observation masquerading as heart failure or, more rarely, as cirrhosis of the liver. A *paradoxical pulse* or an unexpectedly low pulse pressure may suggest the nature of the difficulty, but the salient feature of the diagnosis is the combination of peripheral congestion with a small quiet heart.

*Treatment.*—Under these circumstances digitalis is rarely of use and may even be harmful. Diuretics and tapping are helpful temporarily, but *curative* treatment consists only in the removal of enough of the thickened pericardium to release the ventricles from the fibrous bonds which constrain them. Without such relief these patients are condemned to a permanent

and progressive invalidism, while the adequate release of the ventricles will, in more than half the cases, restore the patients to useful life.

**Suppurative Pericarditis.**—Obstruction to the inflow of blood is produced not only by scar, but also by fluid in the pericardium. The degree of obstruction is found to be related to the pressure in the sac rather than to the amount of fluid. The fluid may be pus, blood or serum. Purulent pericarditis offers another therapeutic opportunity: so long as it remains undrained the infection is active and the obstruction often progressive, while timely operation may save life. Purulent pericarditis is not rare and occurs particularly in pneumococcus pneumonia and in osteomyelitis due to the staphylococcus. Certainly it should constantly be in the mind of the physician caring for these disorders. It may show itself by a friction rub, by a continuation of the signs of infection, or by the evidences of cardiac tamponade.

When it is recognized, the preferred *treatment* is surgical drainage, which relieves the tamponade and encourages healing of the infection. Antibacterial drugs and sera, according to current information, should be used as additions to but not as substitutes for surgical operation.

**Hemopericardium.**—An even more dramatic opportunity for the surgical cure of grave heart disease is to be found in those patients who have severe cardiac tamponade as the result of a penetrating wound. Here skillful and opportune surgery may change a dying patient to a well man. Wounds causing tamponade may be made by knife (or other penetrating weapon such as ice pick or scissors) or by bullet. The resulting picture may be that of tamponade, of hemorrhage, or of a combination of the two. It is important to recall that when hemopericardium occurs with great rapidity, as it does in a perforation of the heart, severe tamponade may come about from as little as 300 cc. of blood in the pericardium, presumably because there is no time for the pericardial tissue to stretch. Tamponade, or interference with the dilatation and filling of the heart, usually shows itself by distended veins,

low pulse pressure, feeble heart sounds, and a paradoxical pulse.

There are two essential steps in the *operative treatment* of such a wound: one is the relief of tamponade by emptying the pericardium; the other is the repair of the wound of the heart. There are now on record some scores of these repairs successfully carried out, which are tributes not only to the skill of the operators, but to the acumen of those who recognized the situation and the possibility of its relief.

### GROUP III. REVERSIBLE CHANGES IN THE MYOCARDIUM

**Beriberi Heart.**—This is a form of congestive heart failure associated with vitamin B<sub>1</sub> deficiency:

**Case IV.**—The patient (R. J.), a twenty-three-year-old taxi driver, was admitted to the hospital complaining of inability to use his legs for the previous five days. For the past six years he had consumed habitually a half pint of whiskey per day and for three months prior to entry he had increased his allotment to a pint daily. With the increase in drinking, anorexia developed, and for the last two months his daily food was limited to coffee and two sandwiches. During the two weeks before coming to the hospital he had vomited every day. At the same time he developed lameness and swelling of his feet, weakness, and numbness and tingling of the fingers of the left hand. Five days before admission he became irritable and disoriented and developed hallucinations. After one day in a psychopathic hospital, where he became mentally clear, he was transferred to the Peter Bent Brigham Hospital for further treatment.

Physical examination showed a well-developed, plethoric young man who was somewhat restless. He was able to lie flat in bed without distress. There were purpuric spots of moderate size on the chest and arms. The eyes were normal. The lips were slightly cyanotic. The tongue was red but not smooth. The teeth were carious but the gums were in good condition. There was a moderate distention of the neck veins. The lungs were clear throughout. The heart was moderately enlarged, both to the left and to the right. The cardiac rhythm was regular. At the apex the sounds approached each other in quality. A moderately loud systolic murmur was heard in this area. The blood pressure was 124/62 and the pulse was rapid and bounding in character. A pistol-shot sound was heard over the femoral artery. The liver edge extended two fingers below the right costal margin. There was a coarse tremor of both hands and definite weakness, more marked on the right. All movements were incoordinated and uncertain. Reflexes in the upper extremities were present but diminished. The legs showed marked edema of the ankles. There was marked weakness of all muscle groups in these extremities

and incoordination on attempting movements. The reflexes were absent but objectively the sensation was not grossly impaired.

Laboratory studies showed a hemoglobin of 72 per cent (Sahli) and a red blood cell count of 3,740,000 per cu. mm. A stained smear showed slight hypochromia and moderate change in size and shape of the red blood cells. Studies of the urine showed it to be normal. The total protein was 5.7 gm. per cent with an albumin of 2.9 gm. per cent and globulin of 2.8 gm. per cent. The Hinton reaction was negative. The venous pressure was 260 mm. of water, the circulation time (decholin) 13.8 seconds and the vital capacity 2000 cc. The electrocardiogram was normal. The basal metabolism was  $+23$  per cent three days after beginning therapy. A seven-foot film of the heart showed the transverse diameter of the heart to be 16 cm. with an internal diameter of the thorax of 29.2 cm. There was moderate pulmonary congestion around the hila and in the right base.

The patient was placed on a high vitamin diet which was supplemented by thiamin chloride and yeast tablets. Under this therapy there was a rapid and dramatic improvement in his condition. By the tenth day in the hospital the edema had completely disappeared and the patient was free from symptoms except for weakness and unsteadiness of his legs. At this time laboratory studies showed that the hemoglobin and red blood cell count had returned to normal. The total protein was 6.8 gm., though the albumin and globulin fractions were still essentially the same. The venous pressure was 123 mm. of water (a normal figure), the circulation time 16.0 seconds, the basal metabolic rate  $+5$  per cent, and the vital capacity 4000 cc. A repeat film of the heart showed it to be of essentially normal size, the transverse diameter being 12.9 cm. and the lung fields clear. The electrocardiogram showed an increase in the size of the T waves.

The remarkable recovery of this patient serves to emphasize the importance of establishing the presence of this type of heart failure, which represents an extreme form of a specific deficiency of the vitamin  $B_1$ . It may arise as a result of an inadequate diet; or an inability to absorb or use this element of the diet may be a cause of this deficiency.

*Cardiac Manifestations of Vitamin  $B_1$  Deficiency.*—These have been described by Keefer<sup>9</sup> and by Weiss and his associates.<sup>10</sup> The recognition of this cause of heart failure is

primarily dependent upon a history of dietary deficiency. The *objective signs* are mostly those of right ventricular failure, such as distention of the veins, elevation of the venous pressure, dilatation of the heart (relatively more to the right), enlargement of the liver, and peripheral edema. That there may be some element of left ventricular failure is indicated by the decrease in vital capacity. Not in keeping with the usual evidences of heart failure are the *peripheral dilatation*, the *high pulse pressure*, and the relatively *rapid circulation time*. These suggest hyperthyroidism and should serve to arouse the suspicion of an unusual situation, more particularly since the basal metabolic rate is not usually elevated. After treatment is begun there may be an increase in the oxygen consumption as in this case. Suggestive but not definitive evidence is offered by the electrocardiogram. The principal change is a decrease in the electromotive force.

*Treatment.*—The treatment of this condition consists of an adequate diet high in the vitamin B factors, with additional amounts of vitamin B<sub>1</sub> (thiamin) given parenterally. Under such therapy, improvement, as in the case described, should be rapid.

It is probable that the congestion of the gastro-intestinal tract and anorexia associated with heart failure in other types of heart disease may also lead to minor degrees of this deficiency. Cases are on record in which the administration of vitamin B<sub>1</sub> has seemed helpful.

**Myxedema Heart.**—Whether or not myxedema is a cause of cardiac failure has been a subject of considerable controversy. However, it is generally agreed that myxedema may produce certain effects upon the heart. These are moderate dilatation (of all chambers) pericardial effusion, bradycardia, and interference with conduction. In addition, the electrocardiogram may show decrease in the amplitude of the complexes and inversion of the T waves.

It is perhaps doubtful if marked congestive heart failure ever results from myxedema alone. Nevertheless, the effects of lack of thyroid on the activity of the heart muscle may play

a part in the production of failure. In any event, the administration of *thyroid extract* brings about striking changes. In addition to the relief of myxedema, there will be noted a decrease in the size of the heart and a reversal of the changes in the electrocardiogram. There may be improvement in the signs and symptoms of failure which presumably may be due to an improving myocardial function.

However, in treating patients in the *older age group* with thyroid extract, a word of warning is not amiss since the heart may be injured more easily by too much than by too little. The use of large doses of thyroid extract will bring about a rapid rise in the basal metabolic rate and prompt relief of the symptoms of myxedema, but under such circumstances there may occur attacks of angina pectoris and occasionally coronary thrombosis. To avoid such alarming complications it is wise to begin on *small* doses, increasing the amount gradually over a period of a month to six weeks until a proper level has been attained.

#### COMMENT

Each of these cases is an example of heart disease in which the cause of progression or disability was removed by treatment. The results were such that it does not seem out of place to describe such patients as suffering from curable heart disease. This clinic is then a demonstration of the value of a positive attitude toward the treatment of heart disease, *i. e.*, of considering the *possibility of cure* in all patients with cardiac disorders. In the present state of knowledge this possibility in most cases does not exist, but it should always be sought.

In several of the cases the successful therapy consisted in the removal of a burden or a handicap. Two points are to be made about this group: first, the more severe the burden or handicap, the greater the improvement to be expected from its removal; second, when a burden is an important factor in heart failure, the failure itself, though it may influence time and method, should not constitute a bar to the therapeutic procedure.



The most important diagnoses are those of conditions which can be effectively relieved by treatment. Therefore, the *complete* and *accurate* diagnosis of heart disease, far from being academic, is of the highest practical importance. Moreover, these diagnoses can usually be established by relatively simple methods. Probably the most important point of all is to have constantly in mind that heart disease *may be curable*.

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## CLINIC OF DR. A. W. CONTRATTO

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### THE SALIENT FEATURES OF AORTIC STENOSIS AND HOW IT DIFFERS FROM THE CLINICAL MANIFESTATIONS OF OTHER VALVE LESIONS

CALCIFIED aortic stenosis is being recognized more and more as a cardiac lesion of rather frequent occurrence. It is responsible, at least in part, for symptoms which are not common to other valvular lesions. There are two schools of thought as to the etiologic factors involved in its production. One believes that it is the result solely of a calcium deposit on the valve without a predisposing cause, other than arteriosclerosis, while the other is persuaded that it is the end result of previous endocardial inflammation, namely rheumatic fever. If careful inquiry is made, one elicits a history of rheumatic fever in 40 to 50 per cent of these cases. It is probable that both conditions are a factor in the production of aortic stenosis.

Aortic stenosis occurs or manifests itself in almost any age group, from the young person in the "teens" to the very old. However, the *average age* at the time of diagnosis is about fifty-two years. It occurs in both males and females but is three times more prevalent in the former than in the latter.

Several clinical histories of patients suffering with this disease will be presented in order to illustrate its salient features more clearly and precisely.

Case I.—W. T., male, aged fifty-four years. When this patient was first seen he had had a known "leaking valve" for ten years. His symptoms were dizziness, severe at times, with attacks of syncope on exertion. The syncopal

attacks occurred at irregular intervals and varied from a feeling of having "a sinking sensation with fog before the eyes," to a complete loss of consciousness lasting one to ten minutes, during which time there were no convulsive seizures. On exertion he complained of substernal pain which radiated to the neck. This pain would abate on rest.

*Physical Examination:* The patient was a well-developed and nourished male, who could lie flat without discomfort. There was no obvious dyspnea or cyanosis and the vital capacity was 4200 cc. The heart was moderately enlarged, the rhythm was regular, and the rate was 72 beats per minute. A moderately loud, rough systolic murmur was heard over the entire precordium, but was loudest over the aortic area. No diastolic murmur was audible, but the second aortic sound was absent. A systolic thrill was felt over the base of the heart when the patient was in the sitting position and after a held forced expiration. The blood pressure was 110 systolic and 70 diastolic. The lungs were clear and there was no peripheral edema.

This patient was followed for a period of six years. During this time he continued to have infrequent attacks of syncope, often injuring himself when he fell. He also continued to have moderately severe angina pectoris. He died suddenly while at work six years after he was first seen. At no time did he have congestive heart failure.

*Case II.*—S. M., male, aged fifty-six years. This patient had had rheumatic fever at the age of twenty-two, at which time he was confined to a hospital for several months. When he was thirty-one years old, he was told during a routine physical examination that he had a "heart murmur." However, he carried on with his occupation and usual routine without any discomfort whatsoever until one year before admission to the hospital at the age of fifty-six. At this time he experienced severe substernal pain on exertion which quickly abated on rest. Shortly after this he had several attacks of syncope without obvious cause. Six months before entry to the hospital, dyspnea on exertion and edema of the ankles were noticed. These symptoms continued to progress until admission.

*Physical Examination:* The patient was obviously ill. There was marked dyspnea and orthopnea. The heart was only slightly enlarged to percussion. The rhythm was regular and the rate was 96 beats per minute. Many moist râles were present at both lung bases. There was marked pitting edema of both ankles and moderate edema of the sacrum. The patient died in congestive failure two days after admission.

*Case III.*—C. B., male, aged forty-six years. This patient was healthy until two years before admission when he noticed a severe clutching sensation beneath the sternum, which radiated to the neck. This pain was typically related to exertion but was never too incapacitating. Six months before admission, following a cold, he began to experience dyspnea, swelling of the

ankles and a cough. These symptoms became more and more progressive until his entry to the hospital.

**Physical Examination:** The patient was markedly dyspneic. The heart was moderately enlarged, with a regular rhythm and moderately rapid rate (92 beats per minute). A moderately loud, rough systolic murmur was heard over the aortic area and to a lesser degree over the rest of the precordium. Over the aortic area there was also present a soft short diastolic murmur. The second sound was absent. Many moist râles were heard over both lung bases, and there was marked edema of the legs and ankles. Fluoroscopy of the heart showed a calcified aortic valve.

This patient died several days later from congestive heart failure. At autopsy the heart was found to be enlarged and weighed 780 gm. The aortic valve was markedly stenosed and calcified. The coronary arteries were normal except for an occasional noncalcified plaque that did not encroach on the lumen.

#### COMMENT

**Symptoms and Signs.**—The predominating complaints in Case I (W. T.) were *dizziness*, *syncope* and *precordial pain*. Dizziness and syncope are rather frequent complaints in patients suffering with aortic stenosis. Occasionally these symptoms are incapacitating, although the patient may have no other cardiac complaints whatsoever. The cause of these symptoms is unknown, but they probably are due to cerebral anemia resulting from the disturbance of blood circulation through the aorta. However, the simultaneous occurrence of a sensitive carotid sinus may be responsible in some cases. The frequent occurrence of dizziness and syncope in aortic stenosis helps to distinguish the condition from mitral stenosis or aortic insufficiency, in which these symptoms seldom occur.

It is to be noted that all three patients had symptoms not unlike the precordial pain of angina pectoris due to coronary sclerosis. However, the high incidence of this complaint in patients with aortic stenosis (about 33 per cent), and the frequent finding of normal or only slightly diseased coronary arteries (Case III) at postmortem examination, suggests that this symptom is due to some cause other than coronary sclerosis. It is well known that a fair percentage of persons having

aortic stenosis die suddenly without ever having had cardiac decompensation (Case I). Probably if more careful histories were taken it would be elicited that many patients who die suddenly with aortic stenosis have previously had symptoms of angina pectoris. Angina pectoris is a rare symptom in patients suffering from mitral stenosis, and when this symptom is present, in all likelihood the stenosed mitral valve is in no way responsible for its production. Likewise, true angina pectoris is rare in patients suffering from aortic insufficiency unless it is of a syphilitic etiology and there is narrowing of the coronary ostia.

The course of aortic stenosis is slow and progressive. In many instances a history is obtained of a person known to have had a *heart murmur* for many years before any cardiac symptoms develop (Case II, twenty-five years). In some cases, some years after an attack of rheumatic fever only a faint systolic murmur may be heard at the aortic area, but as time goes on the murmur becomes louder and louder as more calcium is being deposited on the aortic leaflets. Meanwhile the aortic valve is becoming more and more stenosed. Somewhere in this course of events a *systolic thrill* manifests itself. The thrill, like the murmur, becomes more apparent with the passage of time. Many years after the appearance of a slight systolic murmur at the aortic area, the classical signs of aortic stenosis appear. This, too, is in contrast to aortic insufficiency and mitral stenosis, which in a number of instances manifest themselves much sooner after the attack of rheumatic fever.

**Physical Findings.**—The physical findings in aortic stenosis are quite characteristic. *Cardiac hypertrophy* is almost invariably present in well-marked cases, and can usually be made out on physical examination. However, it must be remembered that although the true cardiac musculature hypertrophy may be rather marked, the size of the cardiac silhouette is not greatly increased. The *heart rhythm* is usually regular, unless some other factor has come into play. This is in contrast to mitral stenosis, in which auricular fibrillation is a

common sequel. There is present a *systolic murmur* of varying intensity, from moderately loud to loud and rough, heard all over the precordium, usually loudest over the aortic area. In about one half of the cases a definite *diastolic bruit* is heard, but the aortic second sound is seldom present. A *systolic thrill* may be felt over the aortic area if carefully sought. The best way to feel the thrill is by having the patient in a sitting position, with the examining palm over the base of the heart. The patient should then fully exhale and lean slightly forward at the same time.

*Fluoroscopy* in recent years has become a great aid in the accurate diagnosis of this lesion, as calcium can usually be seen in the aortic leaflets.

Although the typical case of aortic stenosis may have the so-called *plateau pulse* with a low pulse pressure, this is the exception rather than the rule (about 10 per cent). There are many other factors which may simultaneously influence blood pressure and alter the plateau pulse, such as age, arteriosclerosis, aortic insufficiency and hypertension.

**Prognosis.**—The prognosis in cases of aortic stenosis is variable, depending upon the age of the patient and whether or not symptoms are present at the time the diagnosis is made. As has previously been stated, the course of this lesion is slow and progressive. Thus, if one discovers the presence of aortic stenosis in a moderately young person without symptoms of any kind, it can be stated that the prognosis is good, as many such persons are able to carry on their usual routine for years without any symptoms or discomfort. This is in contrast to *mitral stenosis*, in which disease symptoms are frequently present at the time or soon after diagnosis is made. Moreover, it is less common to find patients with definite mitral stenosis, regardless of how well compensated they may seem, who do not have some dyspnea or other cardiac complaint on exertion. The average age at death of patients with aortic stenosis is fifty-two, while that of mitral stenosis is about ten years less. The prognosis is strikingly different in aortic stenosis when the patient has symptoms or signs of congestive

failure at the time the diagnosis is made, as the duration of life after congestive heart failure has developed is usually short—often six months. This, too, differs markedly from patients with mitral stenosis, in that although the aortic stenosis patient may have no symptoms of congestive failure for many years, when they do occur death is but a matter of a few months, while patients with mitral stenosis may go through several bouts of congestive failure with reestablishment of compensation over a number of years before death ensues. When an individual with aortic stenosis complains of precordial pain—angina pectoris—the prognosis as to life is the same as in persons with angina pectoris due to coronary sclerosis.

The *causes of death*, in order of frequency, in cases of aortic stenosis are: congestive failure, subacute bacterial endocarditis, coronary thrombosis, and an unknown factor resulting in sudden death and having probably the same mechanism that causes sudden death in patients with angina pectoris due to coronary sclerosis.

#### SUMMARY

Aortic stenosis occurs more frequently than was previously thought true. The incidence of angina pectoris is high in patients with aortic stenosis, and it need not be due to coronary sclerosis. These patients are subject to sudden death. Dizziness and attacks of syncope are often present, the exact mechanism of which is unknown. The etiologic factors are probably multiple, but certainly rheumatic fever is an important cause. A person may have well-marked aortic stenosis for many years without cardiac symptoms, but when congestive failure does ensue, the duration of life is relatively short.

## CLINIC OF DR. MARSHALL N. FULTON

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### ACUTE HEMOPERICARDIUM: ITS CAUSES AND CLINICAL MANIFESTATIONS

THE dramatic circumstances of sudden or instantaneous death invariably arouse curiosity and interest in the possible causes. While this interest may, at times, be purely "academic," the diagnostic acumen of the physician often is put to the test by the occurrence of a sudden unexpected fatality.

We are concerned in this clinic with patients who die as a result of hemorrhage into the pericardial sac, due to a rupture of or bleeding from some part of their intrapericardial circulation. While death in rapidly forming, acute hemopericardium is invariably sudden, it need not be instantaneous. Indeed, study will show that there is commonly an interval of minutes, rarely of hours, between the onset of the collapse that usually is manifest and the final exitus. In other cases, death may occur in an instant, the patient expiring with no more than a gasp.

The *diagnosis* of hemopericardium, because of its extremely brief clinical course, is by no means easy and seldom ever a certainty. That hemopericardium may occur as the terminal event in certain well-recognized conditions, such as myocardial infarction, is important to remember if one is to prophesy its discovery at autopsy. Even in myocardial infarction where rupture with hemopericardium may be considered, autopsy may not reveal this or any other condition to explain satisfactorily the sudden death that has occurred. Un-



der these circumstances, death is attributed, usually, to ventricular fibrillation or to powerful nervous stimuli (vagal inhibition) producing sudden asystole. Again, the occurrence of a large pulmonary embolus from the right heart or from an unrecognized thrombophlebitis may result in death quite as sudden in character as that seen with hemopericardium. For these reasons, an opinion as to the final cause of death, even when hemopericardium is a likelihood, must be, in part, speculative, though based on the possibilities presented by the pre-existing disease.

The mechanism producing standstill of the heart in hemopericardium is that of *cardiac tamponade*—a throttling of the heart's action by increased pericardial pressure. Death results, in other words, not from the loss of blood to the circulation, but from the "strangling of the heart" by the distended pericardial sac. It is well known that the degree of distensibility of the pericardium that is compatible with life is variable. It relates to the speed with which the distending medium (usually fluid) accumulates. For instance, in pericardial effusions of rheumatic or tuberculous etiology, as much as a liter or more of fluid may be present in the pericardial sac. The circulation may be embarrassed severely by this accumulation, but may remain adequate for the continuance of life. On the other hand, when fluid (blood) accumulates rapidly, as it does with rupture of even a small aneurysm, or with trauma to a coronary vessel, the heart may cease to fill and empty adequately with as little as 250 to 300 cc. of fluid in the pericardial sac. It is well recognized that it is the pressure within the pericardium rather than the amount of fluid present that determines the shutting off of the circulation.

In the type of acute hemopericardium that concerns us in this clinic, there is not sufficient time for the signs of cardiac tamponade to become manifest. It is for this reason that *accurate* diagnosis of the condition is difficult. None the less, hemopericardium is more than just a pathologic curiosity, and can be suspected by the astute clinician who is aware of the conditions in which it may occur.

We shall turn now to the causes of acute hemopericardium, the manifestations attendant upon its occurrence, and the manner of death which results from it.

#### CARDIAC RUPTURE FOLLOWING CORONARY OCCLUSION AND MYOCARDIAL INFARCTION

The commonest *cause* of hemopericardium is the rupture of a myocardial infarct. This is by no means an unusual mode of death for patients who die as a result of coronary occlusion. Approximately one out of every eight patients who succumb within three weeks' time following obstruction of a coronary artery, die as a result of rupture of the myocardium. Furthermore, the instances in which the ventricle ruptures as a result of any condition *other* than infarction are rare. Krumbhaar and Crowell,<sup>1</sup> in 1925, reviewed the subject of "Spontaneous Rupture of the Heart." In their studies on 654 cases they found that, in the great majority, rupture was due to antecedent coronary disease with thrombosis and infarction. These authors seriously questioned that the former popular diagnosis of fatty degeneration or "ulceration" as a cause of rupture was correct, save as this may be related to infarction resulting from coronary disease. In 257 of the cases which they reviewed, the left ventricle was the site of rupture in 225, the right in only 32. The anterior wall of the left ventricle was three times as commonly the site of rupture as the posterior wall.

The following report offers a typical illustration of the course and manner of death in instances of this type:

Case L.—C. McW., a seventy-year-old man, was admitted to the Peter Bent Brigham Hospital because of pain in the chest. For several years he had had mild anginal pain on effort. Six days before admission, while walking on the street, he developed a burning sensation beneath the sternum. There was an associated numbness, followed by pain in the right arm. Five hours after this there occurred a severe, "crushing," substernal pain which persisted, and with this he experienced a sensation of impending disaster. The chest pain continued in spite of frequent hypodermic injections, and because of this he was advised hospitalization.

Physical examination revealed a pallid, slightly cyanotic patient. The heart was questionably enlarged, showed a rate varying from 80 to 100, and a regular rhythm except for occasional extrasystoles. The heart sounds were distant, approached each other in quality, and along the left sternal border there was audible a to-and-fro pericardial friction rub. The blood pressure was 120/80. There were a few râles in the lower left axilla, but no other signs of congestive heart failure. The white blood count was 8,500, the temperature 99.2° F. by rectum. Electrocardiograms showed abnormal ventricular complexes in Leads II and III, with high take-off and inverted T waves.

The patient was looked upon as having coronary occlusion, and was given morphine for relief of his pain. At ten o'clock on the morning after admission he was comfortable, his blood pressure was unchanged and his condition seemed quite satisfactory. About half an hour later, it was discovered that he had become comatose, with slow respirations, an imperceptible pulse, and barely audible heart sounds. The blood pressure could not be obtained. Caffeine, oxygen, and finally intracardiac adrenalin, were administered without effect and the patient died at 11:35 A. M., fifty minutes after he had been found to be in a state of collapse.

At autopsy the pericardial sac was found to be full of fluid and clotted blood. The heart weighed 430 gm. On the posterior wall of the left ventricle there was an area of softening approximately 6 by 7 cm. in size. Near the upper border of this, 2.5 cm. from the intraventricular sulcus, there was a tear 3 mm. in diameter entering the cavity of the left ventricle behind the papillary muscle. The path of the tract leading from the endocardium to the epicardium was found to be irregular and tortuous, winding from the endocardium upward. At both ends it measured approximately 3 mm. in width, being somewhat wider than this in its course through the heart muscle.

This patient illustrates in a typical way the *course of events* that occur with coronary thrombosis, infarction of the heart, necrosis and rupture of the heart wall and death from hemopericardium. In this instance, the lethal event occurred *six days* after the acute coronary attack, which falls within the period when rupture is likely to occur. It is during the stage in which necrosis and softening of the infarcted muscle is predominant that rupture commonly takes place. Mallory, White and Salcedo-Salgar<sup>2</sup> have shown that the histologic evidence of necrosis can be found in infarcts of heart muscle as early as five or six hours after obstruction of the blood supply has occurred, and that necrotic tissue is most prominent, histologically, from the second to the sixth day. In their series of eight patients who died as a result of rupture of a myocardial infarct, the shortest time following coronary occlusion

was one day, the longest twelve, the average time being six days. In a series of seventeen patients in the Peter Bent Brigham Hospital, who died of a similar cause, death occurred in all instances but one within seventeen days from the time of the onset of symptoms indicating coronary obstruction. The average period was nine days. The single exception to this was a man sixty-three years of age who lived for six weeks after a typical coronary attack before rupture took place.

This point regarding the *time-interval* has two important, practical aspects. It first of all emphasizes the importance of *absolute rest and quiet* during the critical period when rupture is apt to occur, namely, during the first two weeks following the acute attack; in the second place, it is helpful to realize that once a patient has weathered the storm of this two weeks' period, the likelihood of death from rupture is greatly lessened.

The case history detailed above also illustrates that *death following rupture* of an infarct *need not occur instantaneously*. While "sudden" in the sense of occurring within minutes after an acute episode of collapse, there was an interval of nearly an hour before respirations finally ceased. This period of time is found to vary considerably when one observes the course of events in a series of cases. It, doubtless, relates to the speed with which the pericardial sac becomes filled with blood. A myocardial infarct, when it ruptures, does not often "blow out" in the sense of giving away in entirety. There may be a rent 2 or 3 cm. in length which, obviously, would allow for rapid outpouring of blood. Death in such instances is commonly sudden, the patient expiring in an instant. In other cases, the sinus tract is small, measuring no more than 1 to 2 mm. in width. When this is true, as in Case I, the final exitus may not take place so quickly.

Krumbhaar and Crowell<sup>1</sup> made a careful analysis of the terminal symptoms and manner of death in their own cases and many of those reported in the literature. While 81.5 per cent of 400 patients died within an hour of the time rupture

was thought to have occurred (72 per cent having died "suddenly"), there remained a considerable number (19 per cent) who survived for a period varying from an hour to as long as eight days. As these authors point out, it is very difficult in these latter cases to assign with assurance the exact time at which rupture has taken place.

The following summaries are of interest regarding the *manner of death* in several instances of myocardial rupture.

Case II.—L. L., a man of fifty-seven years, was under care in the hospital for a severe attack of coronary thrombosis. On the eighth day of his illness he had a sudden return of extreme precordial pain following an enema. He became ashen gray in color, his pulse disappeared, and precordial pain persisted in spite of morphine. The following morning the blood pressure was 75/50, the heart sounds very distant, and a faint pericardial friction rub was audible. The patient became weaker throughout the day and died quietly that evening, thirty-six hours after his terminal collapse had begun. Autopsy showed the pericardium distended with blood. There was a very small rupture of an anterior ventricular infarct immediately to the left of the interventricular septum at its midportion. The defect was just large enough to admit a small probe. Within the ventricle was a mural thrombus which covered over the area of rupture.

This case is of interest in that death occurred after a period of gradual decline lasting thirty-six hours. It is impossible to say at what time rupture occurred. The very small tract might have allowed for the slow leakage of blood over a period of hours, the escape of blood from the heart being further impeded by the mural thrombus which covered the site of rupture. The picture was complicated by the additional factors of mesenteric thromboses with necrosis and perforations of the bowel which had resulted in generalized peritonitis.

Case III\*—J. J. M., a mailing clerk sixty-three years old, had had attacks of rheumatic fever at the age of twenty-eight and fifty-three years, but had not manifested any resultant symptoms of heart disease. About noon-time on the day of admission he noticed a dull, aching pain in the region of the left shoulder which later in the afternoon extended down his left arm to the elbow. It was bothersome but not severe. While walking up a slight

\* This same case was presented by Dr. Soma Weiss before the Massachusetts Medico-Legal Society, Feb. 7, 1940. To be published in The New England Journal of Medicine.

grade on the way to his home that evening, he suddenly, without aura or warning, lost consciousness and fell to the ground. He was brought to the hospital by car, regaining consciousness about fifteen minutes after he had fallen.

On examination he was calm and stated that he felt perfectly well. There was no fever. The blood pressure was 105/70. The heart did not seem enlarged but exhibited the grossly irregular rhythm of auricular fibrillation, with a rate of 100. The sounds were of good quality, and at the apex several observers noted a moderate systolic and a soft rumbling mid-diastolic murmur. There were no signs of congestive heart failure. The leukocyte count was 12,500.

Four hours after admission the heart action was found to be essentially regular with a rate of 60. An electrocardiogram at this time showed a normal sinus rhythm with right axis deviation, premature ventricular beats and a normal fourth lead. The patient seemed to be doing very satisfactorily. Forty-seven hours after admission, while the nurses were counting the apex and radial rate, the pulse was observed suddenly to become imperceptible, the heart sounds simultaneously to be very loud and totally irregular. The patient gave no cry but his eyes became "glassy" and he was unresponsive. A minute later, the house officer could hear no heart sounds but observed occasional gasping respirations. There was no response following the intracardiac injection of adrenalin, and five minutes after the onset of the episode, respirations had ceased.

At autopsy the pericardial sac was tensely distended and contained 650 cc. of blood. The heart weighed 460 gm. On the lateral wall of the left ventricle extending up 6 cm. from the apex was an area of fresh hemorrhagic infarction, in the center of which was a sinus tract appearing as a small slit. A 2 mm. probe readily passed through this into the ventricular cavity. The mitral valve showed classical stenosis with calcification in the thickened free margins of the fused leaflets. There was extensive atheroma of the coronary arteries, with almost complete occlusion in a descending branch of the left circumflex artery.

Interest in this case lies in the occurrence of rupture within fifty-two hours of the onset of symptoms. Necrosis and softening had occurred relatively rapidly, leading to rupture at an earlier time than is usually found after occlusion has taken place. The manner of death, also, was of interest, especially with the fortuitous opportunity for immediate observation. The nurse who heard the sudden onset of the terminal irregularity of the heart noted the unusual loudness of the first few beats following the beginning of the arrhythmia. Reznikoff,<sup>3</sup> under similar circumstances, described the sounds heard over the heart as a "continuous, muffled, low-pitched, rushing rumble . . . , like the sound of water rushing through a bursting

dam." Death occurred within five minutes, though the orifice through which blood escaped from the ventricle was only a few millimeters in diameter. Finally, it is of interest that the patient had both coronary and valvular heart disease, neither of which had produced symptoms prior to his short, fatal illness.

**Case IV.**—A. D., a housewife forty-two years of age, was in the hospital because of pain between the scapulae radiating to the shoulders, which had been present intermittently for about two weeks. There was fever of 101.6° F. by rectum, a rapid (130) regular heart action with sounds of poor quality, râles at the lung bases, and blood pressure of 100/70. The leukocytes numbered 19,000. The patient was semistuporous; at times, irrational. In the early morning of her third hospital day, she was found by the nurse sitting on the edge of her bed complaining of marked precordial pain, which became intensified after she drank a glass of water. Suddenly, the patient was seized with a generalized convulsion, and respirations ceased "almost immediately."

In this instance, autopsy revealed a rent 3.5 cm. in length on the anterior surface of the left ventricle. This lay in the midportion of a sizable infarct, the adjoining myocardium being only 3 mm. in thickness. The heart weighed 400 gm. Two hundred and fifty centimeters of bloody fluid and additional clotted blood were recovered from the pericardial sac.

This patient illustrates the suddenness with which death *may* occur following ventricular rupture, particularly when the tear in the heart muscle is large and the pericardium is rapidly filled with blood.

**Summary.**—One may summarize the facts concerning hemopericardium from ruptured myocardial infarcts as follows: Rupture, if it is to occur, is most likely to take place during the first two weeks following the coronary attack. While death usually is sudden, in the sense that it occurs either instantly or within two to five minutes after an episode of collapse, there may be a longer period, even one lasting hours, before respirations cease. There are no manifestations of rupture in the patients who die instantly that would differentiate them from patients dying from ventricular fibrillation.

#### DISSECTING ANEURYSM

Another condition which terminates not uncommonly with hemopericardium is dissecting aneurysm of the aorta. In-

terest in this condition has been stimulated in recent years by the publication of reports of cases recognized and diagnosed during life.<sup>4, 5, 6, 7</sup> This interest is the more acute because of the present-day prevalence of coronary occlusion, for which dissecting aneurysm is most commonly mistaken.<sup>8, 9</sup> The diagnosis of dissecting aneurysm during life is not easy, but can be made in some instances with reasonable certainty. It is most often missed because of the failure to think of it as a possibility. While occasional patients with dissecting aneurysm in which a circulatory communication becomes established between the dissected sac and the aortic channel may go on to live for months or years, the majority die acutely. In the series reported by Glendy *et al.*,<sup>6</sup> survival among the acute cases averaged four days from the onset of symptoms. In three others, the duration of life was six, eight and fifteen weeks.

**Clinical Manifestations.**—There is not time in this clinic to do more than mention the clinical manifestations of this interesting condition. It is characterized in its onset by a tearing or crushing *pain in the chest*, radiating at times to the back or abdomen, rarely to the shoulders or arms. This pain is frequently associated with a marked feeling of *faintness*. Often syncope occurs. If there is *hypertension*, which is common, the elevated pressure persists in spite of severe prostration or other signs of circulatory collapse. There may be an associated *hemiplegia* if dissection has extended up the vessels of the neck, and on examination there may be a difference in the palpable pulsations in peripheral vessels on the two sides. A *diastolic murmur* is commonly audible over the base of the heart, but the heart sounds often remain of normal intensity. There may be *fever* and *leukocytosis* persisting for several days.

The *electrocardiographic changes* seen with coronary thrombosis are usually not present, and this negative finding may be an important clue to the correct diagnosis.

In some instances the *x-ray examination* may be of help, as pointed out by Wood and his associates.<sup>10</sup> The features are a deformity of the supracardiac shadow, at times an unusual



shadow along the course of one of the branches of the thoracic aorta. Dissecting aneurysm hardly ever arises as a result of syphilitic aortitis. The lesion occurs either in association with arteriosclerotic changes in the aorta or with the condition described by Erdheim as "medionecrosis aortae idiopathica cystica."<sup>11</sup>

**Course and Termination.**—As we have noted, the majority of patients with dissecting aneurysm die within a few days from the onset of symptoms. The commonest cause of death is the rupture of the aneurysmal sac through the adventitia. Inasmuch as most aneurysms of this type begin in the first part of the ascending aorta, rupture into the pericardial sac is very common, 70 per cent of "acute" cases terminating in this manner.<sup>12</sup> The mode of death in such cases is commonly described as "sudden" or "immediate," meaning that death occurs within seconds or minutes from the time of the observed collapse.

The following two accounts of cases are illustrative of the *terminal picture* that may be seen in dissecting aneurysm rupturing into the pericardial sac. Both patients were seen for but a very short time, so that an adequate study of their condition was not obtained:

**Case V.**—W. R.,\* a sixty-six-year-old banker, was considered to be in good physical condition. There was a history of hypertension but no previous cardiac disorder. On the evening of admission he was stricken suddenly, while leaving a theatre, with a feeling of oppression beneath the sternum. His companion noted that he became very pale, his hands cold and clammy, and that his pulse rate was slow. Fifteen minutes later there occurred, with sudden onset, a very severe pain in the left arm. The radial pulse could not be obtained.

The patient was admitted promptly to the hospital as an emergency case. He arrived in a state of circulatory collapse. The heart action was slow and regular, the sounds somewhat distant. A to-and-fro murmur could be heard at both the apex and base of the heart. Though a pulsation could be felt in the left subclavian artery, there was no pulse obtainable in the left axillary artery or distal to this. The blood pressure in the right arm was 90/60. The patient was considered to have an embolus lodged in the first portion of the left axillary artery. Soon after admission to the hospital he complained of

\* The author is indebted to Dr. Elliott C. Cutler for permission to include this case.

recurrence of substernal pain and of great difficulty in breathing. He immediately lost consciousness, became pulseless in the right arm, and cyanotic. The murmurs previously noted were no longer audible and the heart sounds completely disappeared. Within three minutes of the beginning of this episode, he was dead.

At autopsy the cause of death was found to be a dissecting aneurysm which had ruptured through the adventitia into the pericardial sac, about 1.5 cm. above the aortic valve. The dissection had extended the entire length of the aorta, had involved all of the branches coming off the aortic arch, and had burrowed into the walls of the left subclavian and axillary arteries, terminating in a sharp line at the distal end of the axillary artery which was compressed at this point. The pericardial sac contained 350 cc. of bloody fluid.

Case VI.—J. W. M., a seventy-three-year-old man, had been known for some years to have an elevated blood pressure. On the morning of admission, while attending his furnace, he was heard to utter a cry. His wife came immediately to his assistance and found him lying on the floor, semiconscious, muttering unintelligible words, and with apparent paralysis of the left arm. He seemed to complain of abdominal pain. A doctor was called who diagnosed his condition as cerebral hemorrhage and advised immediate hospitalization.

The patient was unconscious at the time of admission to the hospital. He was breathing stertorously. It was noted that the heart impulse was of moderate force, the heart sounds of very good quality. There were no murmurs. The blood pressure, unfortunately, was not recorded. Cyanosis increased, the pulse at the wrist became imperceptible, and death followed ten minutes after his admission to the ward, too soon for adequate observations to be made.

There was found at autopsy a rent 3 cm. long at the root of the aorta, from which a dissecting aneurysm had formed that extended up both carotid arteries to the level of the mandible, and downward to the iliac vessels. The adventitia had ruptured into the pericardial sac which contained 600 cc. of blood. There were marked arteriosclerosis of the aorta and hypertrophy of the heart muscle.

These brief accounts are characteristic of the course of dissecting aneurysm terminating in rupture. For more details of the clinical history and findings in comparable cases, the reader is referred to the recent literature cited above. In conclusion it should be emphasized that the likelihood of death from rupture of a dissecting aneurysm is always to be feared, once the diagnosis has been established. Sudden exitus may occur if the aneurysm ruptures into the pleural space, the mediastinum or abdominal cavity, as not uncommonly happens. The prevalence of death from hemopericardium in this condi-

tion is due to the great frequency with which the initial lesion occurs in the first portion of the aorta.

### MYCOTIC ANEURYSM

Localized mycotic aneurysms of some portion of the intrapericardial circulation not uncommonly terminate life by producing hemopericardium. Originating as they do from bacterial vegetations, such aneurysms may burrow along the walls of the aorta or pulmonary artery or through the heart muscle, eventually perforating into the pericardial sac. Their recognition during life is by no means easy. Much more frequently they are found as a surprising revelation at autopsy. The same thing is true of the rare instance of abscess formation in the heart wall, such as occurs in septicemia, in which rupture into the pericardium may bring about sudden death.

The following case is a typical illustration of the occasional termination in bacterial endocarditis with mycotic aneurysm:

**Case VII.**—A. D., a fifty-nine-year-old Italian male, was admitted to the medical service of the hospital because of uncontrollable hiccoughs which he had had for one week. He gave a history of slowly progressing cardiac insufficiency over a period of years which had called for constant digitalization for the past four years. In spite of this handicap, he had been able to be about his work until a week before admission. He appeared extremely ill. There were present the classical signs of aortic stenosis, with cardiac enlargement, and a moderate degree of congestive heart failure. Later he was found by x-ray to have a dense mass of calcification in the aortic valve, cardiac enlargement with left ventricular hypertrophy, and rather marked tortuosity of the aorta. Electrocardiograms were not remarkable and included a normal fourth lead.

The patient was on the ward for twelve days. He ran an irregular temperature between 100° and 103° F., and a leukocytosis was present (24,000 cells, with 90 per cent polymorphonuclear cells). In view of his cardiac lesion and fever, bacterial endocarditis was, of course, considered. Four blood cultures, however, were negative. On the twelfth day in the hospital he had a severe shaking chill and complained of intense precordial pain which had begun suddenly and which radiated down the left arm and into the hand. Neither his pulse nor blood pressure could be obtained. He became markedly cyanotic, his respirations grew labored, and within about fifteen minutes from the onset of the chill and pain he was dead.

The sudden exitus led observers to the opinion that the patient had died either from pulmonary embolus or coronary thrombosis. To the surprise of

everyone, it was found at autopsy that the pericardial cavity was filled with 400 cc. of blood. The exact nature of the cardiac lesion was revealed as bacterial endocarditis engrafted on stenosed and calcified aortic valves. This lesion had ulcerated into the myocardium, the blood had dissected up along the pulmonary artery which had ruptured, producing hemopericardium with death from cardiac tamponade.

Two other instances of sudden death from rupture of a mycotic aneurysm into the pericardium have been observed at this hospital within recent years. One occurred in a patient with staphylococcus septicemia arising from a trivial local lesion of the elbow, the other in an elderly woman with a slowly resolving pneumococcus pneumonia. In neither instance was the aneurysm suspected during life. In both cases, death occurred suddenly and without warning. In both, the aneurysm was located in the first portion of the aorta, rupturing into the pericardial sac. This cause of death should be considered in patients, particularly elderly patients, with bacterial infection who die suddenly and unexpectedly.

#### DEATH FOLLOWING PERICARDIAL TAP

The distressing aspects of pericarditis with pericardial effusion often present a pressing problem and demand the important decision of whether or not paracentesis shall be employed. That this procedure may at times be life-saving is undeniable. Because of its inherent *dangers*, however, the decision to perform a tap should always be based on carefully weighed evidence and judgment as to its necessity. Fatalities resulting from puncture of the heart or from nicking a coronary vessel are well known, and unless the evidence of considerable pericardial fluid is unequivocal, pericardial tap should not be undertaken. The following case illustrates a fatality with pericardial tap resulting from puncture of the ventricle, even though no large coronary vessels were injured by the exploratory needle:

Case VIII.—C. E., a forty-seven-year-old laborer, was in the hospital because of severe congestive heart failure, with bilateral hydrothorax, ascites and extensive edema. There was evidence pointing strongly to an accumula-

tion of pericardial fluid, though the etiology of the pericarditis was not clear. The patient was not improving under the usual measures of treatment, including thoracentesis and phlebotomy, and an exploratory pericardial tap was advised. A needle was introduced just below and to the left of the xiphoid process, directed upward and medially. When it had been passed the estimated correct distance, the stilet was withdrawn and venous blood came from the needle in a pulsatile stream under considerable pressure. The needle was withdrawn promptly. Almost immediately the patient threw back his head in spasm, became cyanotic, kicked violently several times, and within less than twenty seconds was dead.

At autopsy it was found that the path of the needle passed through the wall of the right ventricle about two-thirds of the way from the apex to the auriculoventricular groove. Careful serial slicing of this portion of the ventricle revealed that the tract had not traversed any large coronary vessels, but that, as a ragged opening 3 mm. in diameter, it had gaped sufficiently to allow rapid outpouring of blood. Death was due to cardiac tamponade, the pericardial sac containing a blood clot weighing 400 gm. and an additional 500 cc. of blood-tinged fluid. The cause of heart failure was mechanical—an extreme grade of mitral stenosis which had produced only equivocal signs during life.

The dangers of a pericardial tap as illustrated by this case should be remembered whenever this type of paracentesis is attempted. There is, of course, less likelihood of damage from puncturing the ventricle when a large effusion is present, and experience favors the left lateral approach to the one used in this instance. However, even if ventricular puncture is not made, there is danger from injury to coronary vessels on the surface of the heart—an injury that may result in fatal hemopericardium.

There are a number of other conditions, albeit relatively rare ones, that may result in death from acute hemopericardium. *Syphilitic aneurysms* of the aorta occasionally terminate life by rupturing into the pericardial sac. *Trauma*, of course, from stab or bullet wounds is a not uncommon cause. There are a number of reports in the literature,<sup>1, 18</sup> of *rupture of the auricle of the heart*, which like ventricular rupture is nearly always secondary to infarction; of *rupture of a coronary artery* secondary to an arteriosclerotic lesion<sup>14</sup> or to periarteritis nodosa.<sup>15</sup> *Chronic lesions* involving the pericardium or heart wall—neoplasm, tuberculosis, rarely syphilitic gumma—may, any of them, result in bleeding into the pericardial cavity. It

is more usual in such conditions for effusion to be present, into which oozing of small amounts of blood has occurred.

### SUMMARY AND CONCLUSIONS

Sudden death from the rapid accumulation of blood in the pericardial sac occurs not infrequently. While death in such instances may be instantaneous, there is commonly an interval of minutes, rarely of hours, between the collapse that is usually manifest and the final exitus.

The commonest cause of acute hemopericardium is the rupture of a myocardial infarct. This event, if it is to occur, is most likely to take place during the first two weeks following coronary occlusion.

Case stories are presented illustrating the course and manner of death observed in patients who die with hemopericardium from ruptured infarcts, dissecting aneurysms, mycotic aneurysms, and puncture of the ventricle during pericardial tap.

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THE PERIPHERAL CIRCULATION IN ACUTE INFEC-  
TIOUS DISEASES

IN acute infectious diseases the physician customarily examines the heart, but neglects the peripheral circulation unless there is a complaint referable to the extremities or a question of arterial or venous occlusion. This is unfortunate, because in many patients careful observation of the peripheral circulation gives more useful information concerning the patient's condition than does auscultation of the heart.

**Examination of the Peripheral Circulation.**—To evaluate the condition of the peripheral circulation one palpates the radial and digital pulses, examines with a flashlight the tips of the fingers for capillary pulsations, and looks for a capillary pulse by direct inspection of the nail bed. The arterial blood pressure is measured. The femoral and brachial vessels are auscultated for systolic sounds. The temperature and color of the skin are observed. One notes whether the veins of the extremities are full or empty, and whether they fill rapidly when a tourniquet is applied. The venous pressure is estimated by observing the distance above the heart at which the veins of the hands collapse.

**Normal Response of the Body to Fever and Infection.**  
—The body normally responds to fever and infection by an increase in the metabolic rate and by an increase in cardiac



output. In general, the higher the fever the more rapid the circulation. The rectal temperature must therefore be known in judging the state of the circulation, because a cardiac output that is adequate for a patient with a temperature of 101° may be inadequate for one with a temperature of 106° F. This increased velocity of blood flow is manifested clinically by warm, flushed skin, full bounding pulse, palpable digital pulsations, and systolic sounds over the femoral vessels. The veins of the extremities are dilated, and they fill rapidly when the venous return is obstructed. The pulse rate is elevated and the pulse pressure is either normal or increased. Not all of these signs are present in every case.

#### ILLUSTRATIVE CASES

In some patients with fever and infection, marked arteriolar dilatation is present, although the circulation is adequate. This is illustrated by the following report:

**Case I. Fever of Indeterminate Origin with Very Rapid Peripheral Rate.**—A seventeen-year-old Italian male entered the hospital complaining of chill, fever and jaundice of twenty-four hours' duration. The rectal temperature was 104° F., the pulse rate 120, respirations 25, and the blood pressure 90/20. The skin was hot, dry and flushed. The heart was normal in size and there were no murmurs. The radial pulse was full and collapsed quickly. On palpating the fingers a marked digital pulse was elicited. When the end of a finger was transilluminated by a small flashlight the light flickered with each heart beat because the finger transmitted less light during systole. On applying slight pressure to the nail a marked capillary pulse was seen. The veins of the extremities were full, but they collapsed rapidly when they were raised above the level of the heart.

The patient was given 4000 cc. of fluid daily and a high carbohydrate diet. He made an uneventful recovery, although the etiology of his disease remained unknown. On the fifth hospital day his temperature was normal, pulse rate 80, and blood pressure 110/70.

The clinical picture was typical of a very rapid peripheral circulation in response to fever and infection. The collapsing pulse, the capillary pulsations and the systolic sounds over the femoral and brachial vessels were all manifestations of a *widely dilated arteriolar bed*.

In this case the widely dilated peripheral vascular bed and the moderate fall in arterial pressure did not indicate a serious prognosis, but represented an exaggeration of the usual response of the body to fever. These peripheral signs may be erroneously attributed to aortic insufficiency. It is unfortunate that so much emphasis is usually laid on the peripheral signs of aortic insufficiency because the same signs are found in hyperthyroidism, in anemia, in beriberi and to some extent after exercise, as well as in fever. The collapsing pulse, the capillary pulsations and the pistol shots are merely manifestations of the rapid flow of the blood out of the arterial system and do not indicate whether the change in circulation is due to increased peripheral flow or aortic insufficiency. For the diagnosis of aortic regurgitation one is solely dependent on the demonstration of an aortic diastolic murmur.

The *flushed skin* indicated that the capillaries and small venules were also somewhat dilated. By physical examination it is usually possible to tell whether the arterioles and capillaries of the skin are dilated or constricted. Lewis<sup>1</sup> has reported that the color of the skin depends primarily on the degree of dilatation of the subpapillary venous plexuses and to a lesser extent of the capillaries, and not on the degree of arteriolar dilatation. When a hand is immersed in ice water the skin becomes red. The vessels distal to the arterioles dilate, but the arterioles remain constricted, as shown by the absence of palpable digital pulsations and by the very slow blood flow. When the body is heated, the blood flow to the hand may become very rapid while the skin remains relatively pale. In such a case the primary dilatation is in the arterioles while the subpapillary venous plexuses and capillaries are less affected. Drugs, likewise, may have a selective action on certain vessels. Histamine can be infused intravenously in such quantities that the vessels distal to the arterioles are dilated although the arterioles are not. The skin, therefore, has a cyanotic flush, but the blood flow to the skin is not increased.<sup>2</sup>

It is important to remember that *all the arterioles in the body do not necessarily respond in the same way*. After the

subcutaneous administration of 1 cc. of epinephrine the skin of the hands, feet and face is very pale, indicating that the capillaries and venules in these areas are constricted. At the same time the blood flow in the hands and feet decreases and the digital pulsations are no longer palpable because the arterioles in the fingers have also contracted. However, the blood flow must have become faster in some parts of the body because the cardiac output is increased. This is confirmed by the fact that the diastolic pressure frequently is decreased and that marked pistol shots are audible over the peripheral vessels. Plethysmographic records show that part of this increased blood flow occurs in the muscles.<sup>3</sup>

Patients with acute infectious diseases frequently die from circulatory failure. It is important to realize that *these patients usually do not have congestive heart failure* and that the measures used for treatment of congestive heart failure are useless and may do harm. In certain cases the circulatory failure is clearly peripheral in origin, in others both the peripheral circulation and the heart may be involved. The following cases are illustrative of the types of circulatory failure usually seen:

**Case II. Infection Marked by Peripheral Vasodilatation with Low Arterial Pressure.**—This fifty-nine-year-old, white Italian laborer entered the Peter Bent Brigham Hospital on February 27, 1940, complaining of cough with blood-streaked sputum, and of pain in the right chest for one day. On the day of admission he vomited several times, had some diarrhea, and became irrational.

Physical examination revealed a restless, irrational male who appeared acutely ill. Rectal temperature was 102.6° F., pulse 120, respirations 40, blood pressure 80/52. The skin of the face, trunk and extremities was warm, dry and red. The veins of the extremities were full but the venous pressure was not increased. The radial pulse was small; the digital pulsations were absent. The lungs showed an area of consolidation at the right base.

Laboratory investigation showed the red blood count and hemoglobin to be normal. The urine had a 1+ albumin and a specific gravity of 1.020. Type I pneumococci were obtained from the sputum and blood.

The patient was given a clysis of 1000 cc. of 3 per cent dextrose in saline the night of admission. He received sulfapyridine and Type I antipneumococcus serum, the latter being given intramuscularly.

On the following morning the condition of the patient had shown little change. The blood pressure was 70/40, pulse 140. The skin was still red,

dry and warm and the veins were still full. There were no palpable digital pulsations and no sounds over the femoral vessels. The hematocrit reading was 46.5, and the serum protein was 6.7 mg. per cent.

The patient was given 900 cc. of citrated blood. When the transfusion was finished the blood pressure had risen to 90/60. Two hours later it was 110/70. The patient made an uneventful recovery.

During the first twenty-four hours in the hospital this patient was in shock. The clinical picture was one of marked dilatation of the arterioles, capillaries and veins, in which the arterial pressure was not maintained by a simultaneous increase in cardiac output. As the arterioles were dilated the extremities were warm, the veins filled rapidly from below, and the blood from the antecubital veins was not dark. The skin was red because the vessels distal to the arterioles were also dilated. Thus, peripheral vasoconstriction had not occurred. As peripheral dilatation took place, the cardiac output did not increase sufficiently to maintain a circulation adequate for the patient's needs. This was shown by the low blood pressure, by the absence of palpable digital pulsations, and systolic sounds over the femoral vessels. The circulation, while probably no slower than in a normal person under basal conditions, was inadequate for a patient with fever and infection.

This picture of peripheral vasodilatation without a corresponding increase in cardiac output, and the resulting low arterial pressure, is frequently seen in acute infectious disease. In these cases the prognosis is not as serious as one would predict from the level of the arterial pressure. The prognostic significance of a marked fall in arterial pressure depends on the effort that the body has made to maintain the pressure by vasoconstriction. When the arterial pressure falls after maximum vasoconstriction has occurred, the prognosis is serious; when it falls because of vasodilatation without a corresponding increase in cardiac output, the prognosis is more favorable. In the patient presented here, the circulatory failure was not the result of heart failure, because after transfusion the condition showed marked improvement. Studies on this

and other patients have shown that hemoconcentration may not occur. The disproportion between the blood volume and the size of the vascular bed which produces the fall in arterial pressure is primarily the result of an increase in the size of the vascular bed.

In these cases *transfusions* are indicated because the increase in blood volume produced by transfusion is more permanent than that produced by intravenous saline or glucose. It is probable that serum transfusions would be as satisfactory as whole blood if serum were as readily available. Intravenous administration of 10 per cent *dextrose* in saline may be useful as supportive treatment until blood can be obtained. In this type of collapse, *drugs* which produce a rise in blood pressure without causing an increase in metabolism may be beneficial until a transfusion can be given. Paredrinol or paredrine given intramuscularly in doses of 25 to 50 mg. causes an increase in arterial pressure and does not appear to have any objectionable side effects.<sup>4</sup>

**Case III. Infection Marked by Postural Circulatory Disturbances.**  
—This fifty-two-year-old white male entered the Peter Bent Brigham Hospital on March 20, 1940, complaining of chill, fever and pain in the side, of one day's duration. Physical examination showed consolidation of the right lower lobe. The sputum showed Type I pneumococcus. The rectal temperature was 103.8° F., the pulse 115, and the blood pressure 128/72. The skin was flushed. On sitting up in bed the patient became pale, dizzy, his pulse imperceptible, and he fainted. After lying back his pulse and blood pressure were quickly restored. He was treated with Type I antipneumococcus serum and sulfathiazole.

The following day the rectal temperature was 101.6° F., the pulse 102 and the blood pressure 122/86. The patient's face was slightly flushed, the extremities were warm, and there was a slight capillary pulse. No pistol-shot sounds were heard upon auscultation. On sitting up in bed the patient became pale and complained of dizziness. The pulse rate was 120 and the blood pressure 105/90. On lying down the patient immediately recovered. On March 25, 1940, he was able to sit upright in bed without symptoms and with no fall in arterial pressure. The blood volume was determined when he had symptoms on sitting up, and at a later date when he was symptom-free, and was the same on both occasions.

In this patient the circulation appeared normal in the horizontal position but, when he sat up, the pulse pressure nar-

rowed, the pulse rate increased, and there were signs of a decreased cerebral blood flow. The diastolic pressure did not fall, which indicated that the arterioles were constricted and that the peripheral blood flow had decreased. The rapid recovery on lying down showed that the blood had remained in the blood vessels and that the heart was adequate. The blood volume did not increase as his postural adaptability improved. Thus, his inability to sit up was not the result of a decrease in blood volume.

In the presence of a high diastolic pressure the pallor, the narrow pulse pressure and the faintness were signs of a decreased cardiac output and were produced in this instance by a decreased venous return rather than by heart failure. Because of infection the distensibility of the venous system was increased. When the patient sat upright the hydrostatic pressure in the vessels below the heart was increased and the veins and venules dilated, pooling blood in the abdomen and lower extremities.

If the circulation in the horizontal position appears adequate and if the patient is well hydrated, this type of collapse requires no special *treatment* except to keep the subject flat. A similar clinical picture can be produced by a decrease in blood volume from dehydration or from hemorrhage. In patients whose blood volume is diminished, the pooling of the normal amount of blood by sitting upright may decrease the venous return to the heart sufficiently to produce collapse. If the patient appears dehydrated or if the urine is highly concentrated, more fluids should be given by mouth or parenterally. If the patient is malnourished or anemic, or if the serum proteins are low, transfusions are indicated. In some cases this type of postural collapse can be prevented by the use of paredrinol or paredrine, which produce an increase in venous tone.<sup>4</sup>

**Case IV. Pneumonia with Peripheral Symptoms Due to Progressive Decrease in Cardiac Output.**—A forty-five-year-old white male entered the Peter Bent Brigham Hospital on March 18, 1940, with a history of pneumonia of two days' duration. He was a chronic alcoholic. Physical examination at

4 P. M. revealed a rectal temperature of 105° F., and respirations of 50 per minute. The pulse rate was 150 and the blood pressure 175/105. The patient was apprehensive and restless and appeared acutely ill. The radial pulse was of fair volume. The extremities were warm. The veins filled rapidly and the venous pressure did not seem to be elevated. The lower and middle lobes of the right lung were consolidated. There was a pericardial friction rub but the heart was not enlarged. Sputum and blood culture contained Type III pneumococci.

Sulfathiazole therapy was started immediately. The patient was given a clysis of 1500 cc. of Ringer's solution. At 7 P. M. the blood pressure was 115/78. At 9 P. M. the patient could be aroused with difficulty. The pulse rate was 120, and the radial pulse was weak and thready. The blood pressure was 84/70. The skin was pale, the hands were cold, and the lower extremities below the legs were cold. The veins of the extremities were collapsed. The venous blood from the antecubital vein was dark. There were no palpable digital pulses. The blood volume was within the normal range. At 10 P. M. the patient was given a transfusion of 1100 cc. of citrated blood. At 11:30 P. M. the transfusion was completed. The patient showed no signs of clinical improvement. The blood pressure did not rise. The veins of the extremities became visible and the venous pressure appeared to be elevated. At 11:50 P. M. the pulse rate had dropped to 96. The patient died at 12:05 A. M.

The clinical picture in this patient was one of a progressive decrease in cardiac output. It was characterized by restlessness, sweating, cold, pale extremities, constricted veins, weak, thready pulse, and gradual narrowing of the field of interest. Peripheral constriction of the arterioles had occurred, but in spite of this the cardiac output was not sufficient to maintain the arterial pressure. A similar clinical picture is seen after hemorrhage, the decrease in cardiac output being caused by a decreased venous return rather than by disease of the heart. In acute infectious diseases it is probable that the decreased cardiac output is frequently caused both by increased venous pooling of blood, so that the venous return to the heart is decreased, and by the direct effect of the infection on the heart muscle, which causes it to pump less efficiently. The relaxation of the venous system, combined with the sudden onset of the heart failure, would explain the absence of the usual picture of congestive failure.

Clinically, experience has amply demonstrated that the usual treatment of heart failure by digitalis is worthless in this condition, and that venesection is harmful. It is not

known why digitalis is ineffective. It may be that this type of heart failure is always secondary to the peripheral collapse or that, in the presence of infection, digitalis does not increase the efficiency of the heart.

The *prognosis* in these cases is very poor unless the circulatory collapse is precipitated by some obvious cause, as by the patient sitting up to move his bowels or by an attack of pain. *Therapy* consists of warming the patient, elevating the foot of the bed to increase the blood supply to the brain, and injecting glucose and saline intravenously. Transfusions are indicated because they fill the vascular system and increase the venous return. Many times they will have no beneficial effect. Drugs which act on the nervous system, such as strychnine, caffeine and coramine may be useful. Drugs like paredrinol or paredrine, which act primarily on the peripheral vascular system, usually cause a rise in blood pressure, but the effect is only temporary.

With the rapid advances in chemotherapy, many infections can be brought under control before the circulation fails. It is time to re-study the care in cases of circulatory failure which have formerly been considered fatal and in which therapy has hardly seemed worth while. If the patient can be kept alive by supportive measures until the infection is controlled, the circulation may improve spontaneously.

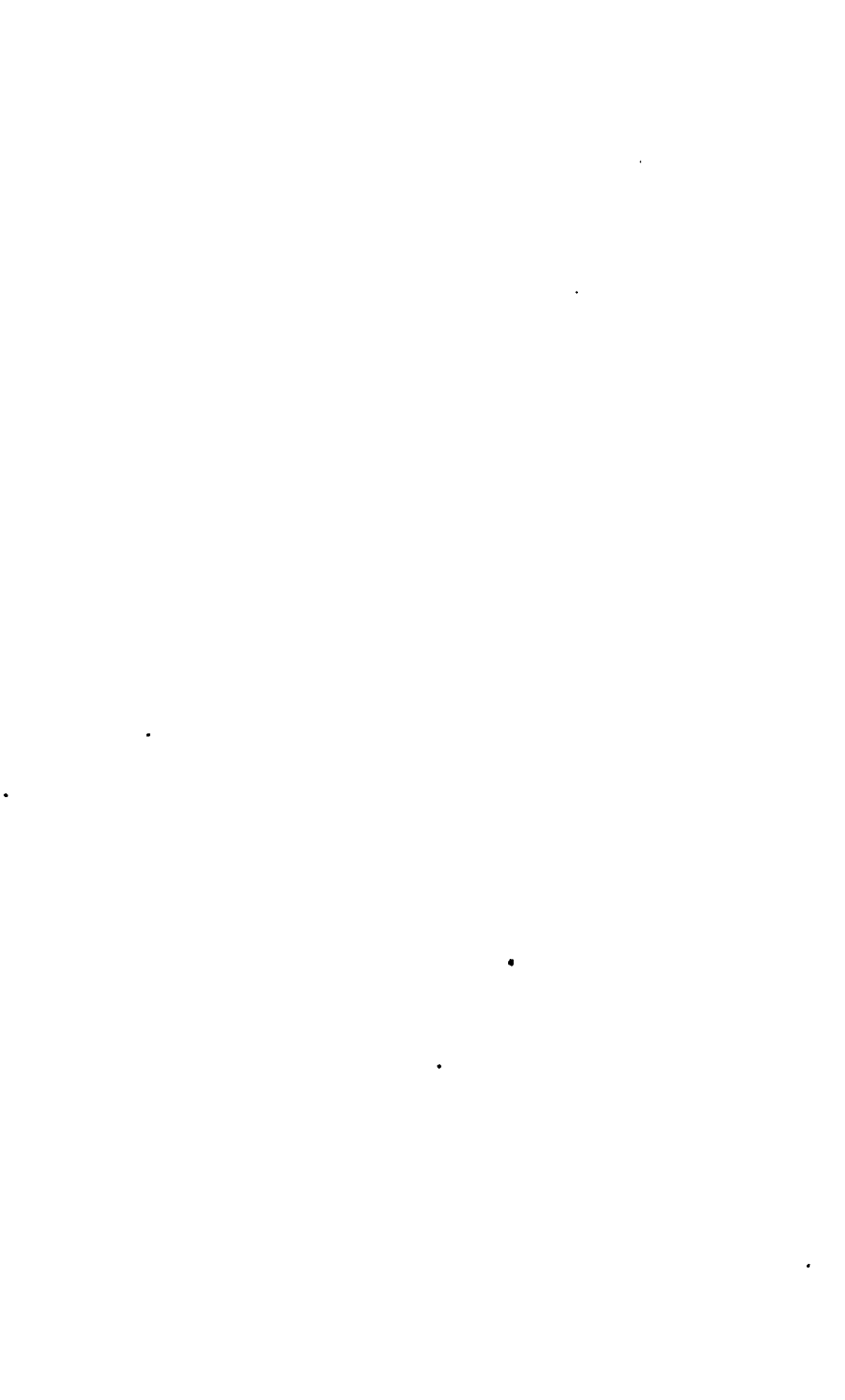
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## SYMPOSIUM ON DIAGNOSTIC HINTS



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#### CLINICAL AXIOMS

Axiom . . . "a generalization based on experience" (Webster).

THE statement that "all generalizations are false, even this one" is as applicable to medicine as it is to anything else, and in the definition given above may be seen one reason why this is so. Physicians practicing in different localities, under dissimilar conditions, and dealing with various types of patients and heterogeneous diseases, inevitably will draw from their respective clinical experience conclusions which are at variance with each other. Thus as has recently been pointed out,<sup>1</sup> an enlarged liver in Changsha is probably due to schistosomiasis, in Peiping to kala-azar, whereas in Baltimore, these are possibilities hardly to be considered. To take a more specific example, a physician in general practice who sees perhaps half a dozen cases of pulmonary tuberculosis during the year will soon make the observation that all of these patients have a blood pressure which is near the lower limits of normal, and he will come to consider this phenomenon a definite part of the clinical picture of this disease. But if he should visit a sanatorium devoted to the care of such patients, and examine the records of several hundred cases, he would experience no difficulty in finding quite a few whose pressure was elevated far above normal.

Thus the maxims or axioms which consciously or subconsciously every practitioner accumulates and stores in his mind as he grows in clinical experience are correct only as based on this experience. As in the fable of the blind men and the ele-

phant, the limited observations of a single man will not usually permit of conclusions which have a universal application. In other words, no medical maxim or axiom is 100 per cent correct, and none is capable of being accepted without reservation. Whether or not there is sufficient justification for the consideration of any such maxim must lie in the determination as to whether or not it is reasonably true in a fair proportion of instances.

**Fundamental Diagnostic Principles.**—No presentation of clinical or diagnostic axioms would be complete without citation of Dr. Blumer's fundamental dicta:

1. When a diagnosis has been reached, all of the symptoms and signs must be compatible with it; otherwise, the chances are that it is incorrect.
2. When there is an apparent conflict between the subjective and objective symptoms, the latter have greater weight in pointing to the diagnosis.
3. A diagnosis of a single disease is more likely to be correct than a diagnosis of more than one disease, provided that it suffices to explain all the symptoms and signs present.
4. When two diseases are possibilities, with apparently equal evidence in favor of each, the chances favor the commoner of the two.
5. Diagnoses reached by exclusion are dangerous and are apt to be incorrect.
6. Do not change a diagnosis reached after careful consideration without very cogent reasons.<sup>2</sup>

If there are any diagnostic axioms which are entitled to the mathematical designation, "self-evident proposition," the six cited above deserve a high place on the list. But like many other truths, they are so obvious that their significance is sometimes not appreciated. The same may be said of the following:

In the diagnosis of a given disease it is essential that the physician rest his opinion, not upon one or two symptoms, but upon a series of symptoms which, when properly put together, give him a complete, or nearly complete, picture of the malady. It is as futile for a physician to attempt to base a diagnosis upon a single symptom as for an architect to attempt to determine the appearance of a house by seeing one of the stones which has been removed from its walls.<sup>3</sup>

The above conceptions are of primary importance in any consideration of the general subject of diagnosis; they are concise and succinct statements of fundamental diagnostic principles. As such, they can hardly be qualified, but extension and amplification of some of their implications may be expressed as corollaries:

*Diagnostic problems often turn out to be instances of a common disease presenting unusual symptoms.* Thus to return to the example given in the first paragraph, a practitioner conceivably might be prejudiced against making the diagnosis of pulmonary tuberculosis in the case of a patient with hypertension—that is, he would consider the former incompatible with the latter. Or, to take another instance, he may have some doubts about a diagnosis of peptic ulcer in a patient with high blood pressure, which is another unusual but perfectly possible combination. When we have a fairly good clinical picture of a given disorder, with one or two bizarre symptoms or signs (*i. e.*, symptoms or signs which either do not fit the textbook descriptions of the disease, or which seem to conflict with or be actually incompatible with the diagnosis being considered), there are two possibilities open to us: Either more than one disease is present; or there is a single disease with unusual manifestations. Usually it is the latter—a “text-book picture” of a given ailment being about as rare a finding as anything in medicine. But it is also true that *the greater the age of the patient, the greater the likelihood that more than one diagnosis must be made in order to account for all of the signs and symptoms.*

Diagnosis is based on a consideration of three factors: the history, the physical examination, and the laboratory findings. Of these, by all odds the most important is the history.

**Importance of the History.**—*It has been variously estimated that in from 60 to 80 per cent of cases, the diagnosis can be made from the history alone.* As Dr. Maurice Richardson used to teach, “*when in doubt about the diagnosis, go back over the history.*” In many cases, *the only clue* to the diagnosis will lie there. It is worth remembering that, usually,

symptoms *precede* demonstrable anatomic changes, and that if we have sufficient acumen to interpret symptoms correctly, our diagnosis need not wait for the appearance of confirmatory physical signs. When these are present, the *combination* of history and physical examination should far outweigh any laboratory findings.

*No history is complete if it concerns itself only with the symptoms. It is the patient, not the disease, which is the entity.* This point is well illustrated by a consideration of the organ neuroses:

The patient complains of the affected organ. Doctors are more than half inclined to believe that organ pathology lies behind the complaint. When some focus of infection or some organic lesion that could lead to reflex disturbances of the autonomic nervous system has been discovered, this is often spoken of as "making a diagnosis." A truer conception of diagnosis would require an estimate of the percentage value of each of a number of concurrent factors, all of which were needed to produce the organ neurosis.<sup>1</sup>

It is only through a careful and painstaking history that an appraisal of the importance of each of these concurrent factors may be arrived at. We may safely assume that a goodly proportion of patients are what is called "psycho-neurotic"; sooner or later, however, they must develop organic disease of some sort. To single out the significant complaints requires inductive reasoning based on a sense of relative values; this can come only from consideration of the patient as a whole, and not merely his complaints.

Among the specific points which a history should attempt to determine are the *patient's individual threshold for pain, his constitutional and psychic diathesis, and whether or not he is under emotional strain sufficient in his particular case to excite an organ neurosis.*

While it is important that the history as elicited by the physician be complete and thorough in the most minute detail, *if the patient himself volunteers such a history, presents himself with a detailed account of his symptoms and, especially, if this account covers a long period of time, this usually suffices to establish a diagnosis of functional disease.* The likelihood

of this being the case is increased if he brings with him a written account of his complaints.

**Laboratory Findings.**—The tremendous growth of laboratory medicine in the past generation or so has led to a tendency to emphasize this aspect of medicine at the expense of the more purely clinical side. It is only recently that there has begun to be a swing of the pendulum back in the other direction. It would be absurd to deny the value of the laboratory to the practitioner of medicine; or to attempt to minimize the very real contributions that have been made to medicine, and which are constantly being made, by the various instruments of precision now at our disposal. The real danger, as has been pointed out by several writers recently, does not lie in the use of the various laboratory and technical aids, but rather in the *undue emphasis* placed on the value of the information they yield.

*No diagnosis based on clinical evidence need be changed, or should be changed, merely because it is not supported by laboratory findings.* To mention a few every-day examples, we know that serious heart disease may be present and yet show no electrocardiographic evidence; that cancer of the gastro-intestinal tract, for instance, may be present and yet not be visible by x-ray; that clinical syphilis has much more weight than negative serology.

Similarly, *diagnoses based on laboratory evidence alone rest on an insecure foundation.* This is excellently exemplified by a case report recently published<sup>6</sup> of a patient who presented symptoms of pulmonary infection, loss of weight, and abdominal pain. The physical findings were consistent with consolidation at one lung apex. The white cell count varied between 51,000 and 135,000, and for this reason a "clinical" diagnosis of leukemia was made. Necropsy revealed bronchiogenic carcinoma; and this, in fact, was the diagnosis made by the physician who discussed the case at the clinicopathologic conference, he basing his opinion purely on the history and the physical findings, and not being misled by what appeared to others as a significant laboratory finding.



When we consider a diagnosis based on the history and the physical examination, we find that *laboratory procedures often confirm it, seldom disprove it, and hardly ever establish it*. Major has stressed the current tendency to neglect the simpler methods of diagnosis for new ones which have recently appeared, the so-called instruments of precision such as the x-ray, the electrocardiograph, and the various quantitative laboratory tests. Some excerpts from his paper will bear repeating here, as they may be made to form a group of important diagnostic axioms:

Inability to walk in the dark and lightning pains in the legs are as important in the diagnosis of *tubes dorsalis* as is the positive Wassermann.

Confronted with a history of increasing sluggishness, inability to keep warm at night in bed, increasing dryness of the hair and roughness of the skin, one can diagnose *myxedema* without a subnormal basal metabolic test.

In many diseases the location and character of *pain* is an important clue in diagnosis. In angina pectoris the physical examination may show nothing. There is no registering device for pain.

Percussion of the heart will demonstrate *cardiac enlargement* better than a study of axis deviation in the electrocardiogram. Percussion will demonstrate lateral displacement of the heart as accurately as the x-ray.

Auscultation of the heart . . . gives better evidence for the diagnosis of *mitral stenosis*, of *aortic insufficiency*, and of the less common lesions than does any instrument of precision.

The glucose tolerance test is not essential to the diagnosis of *diabetes mellitus*. Usually the diagnosis may be clinched by the history and the demonstration of sugar in the urine. . . . It is more important to know whether a patient is secreting sugar during a twenty-four-hour period, and, if so, how much, than it is to know the exact height of his blood sugar at the precise moment that the blood is drawn.

Chemical methods have increased our knowledge of *kidney diseases*, but are not able to diagnose a failing kidney until three-fourths of the glomeruli have been destroyed. In the diagnosis of diseases of the kidney the sheet anchors are still the *sphygmomanometer* and the examination of the urine for albumin and casts.

Pain and chronicity are characteristic of *duodenal ulcer*. Food or alkalis will remove the pain which comes on two to four hours after meals. One need not refuse to treat a patient with duodenal ulcer because x-ray studies and gastric analyses cannot be made.\*

\* The italics are ours.—The Publishers.

There are a few diseases, however, the diagnosis of which requires *great dependence on laboratory procedures*. One of these is early pulmonary tuberculosis, a diagnosis which often can hardly be made without x-ray evidence. Bacteriologic studies are also important in this disease, as they are in differentiating between the various types of pneumococcus infection, streptococcal diseases, and the like. And there are few clinicians today who would have the temerity to make a diagnosis of typhoid fever without confirmatory evidence from the laboratory.

**Significance of Pain.**—It has long been recognized that the *site* at which a patient experiences pain, or the *organ* to which he attributes his complaints, more often than not *is not the seat of his disease*. Dr. W. J. Mayo expressed this dramatically when he stated that 95 per cent of patients who complain of stomach trouble have nothing the matter with their stomachs. The *referred* pains due to diaphragmatic irritation, coronary disease, nephrolithiasis, and duodenal ulcer may be mentioned among the familiar examples of this phenomenon.

**HEART DISEASE.**—If we were to determine the single branch of medicine in which the significance of pain is most often misinterpreted by the patient, it might well be the field of *cardiology*. *The patient who complains of pain in his heart, by which he means precordial pain, almost never has heart disease*. The pain due to actual cardiac disease is experienced substernally, or is referred to neck, shoulder, or arm—it is almost never felt over the heart itself, or over what the patient considers the region of the heart. And the “acute indigestion” which we still see mentioned in the periodical press as a cause of sudden death, while it is usually in reality a coronary attack, whatever it may eventually prove to be, we know it never to have anything to do with digestion or indigestion if it occurs in a patient over forty.

An axiom of cardiology is that *there are no symptoms commonly attributed to heart disease, such as precordial pain, dyspnea, edema, palpitation, or “heart consciousness,” which cannot occur either on a purely functional basis, or as a result*

*of disease elsewhere than in the heart.* A natural corollary to this, then, is that when we are considering the question of heart disease in any patient, the diagnosis should be based more on the physical findings than on the history, and that the history should be considered in the light of the physical findings. When the presence of heart disease is actually established, the history takes on a more important aspect.

Despite a great number of tests which have been suggested as means of measuring the functional capacity of the heart, and of estimating the strength of the cardiac reserve, the best indication of the condition of a heart is the *amount of exertion* required to bring on symptoms. As Mackenzie put it, it is the abnormal facility with which signs of exhaustion are produced, and not the signs themselves, which is the earliest indication of heart failure.

*Angina pectoris in patients under forty-two or forty-three is due to syphilis.* The very few exceptions to this rule will be found in patients who have *rheumatic* heart disease. In either of these types the angina is apt to progress, both in frequency of attacks and in severity, at a much more rapid rate than is angina due to other causes.

*Simple inspection* of cardiac patients will often tell much about the type and extent of their disease: A bilateral malar flush is almost pathognomonic of mitral disease; rheumatic cardiacs with marked pallor usually have aortic valve involvement, although sometimes a concomitant anemia may be as important a cause. The *café au lait* complexion of patients with subacute bacterial endocarditis is much mentioned in the literature, but this may in practice be noted in a much smaller proportion of cases than is the grayish or ashen pallor of aortitis and aneurysm, about which little may be read. This is sometimes striking even in negroes.

Before leaving the subject of heart disease, there are two axioms which may be worth repeating: The first, that a *rheumatic cardiac with dyspnea at rest has either pericarditis or involvement of the lungs*, is offered without further comment. The second is this, that *whenever we note a weak apex impulse*

and a relatively strong pulse beat, we are justified in making a presumptive diagnosis of pericarditis. This is a combination worth watching for, not only in cardiacs, but in patients with pneumonia, nephritis, and tuberculosis.

**Signs of Disease in the Respiratory Tract.**—Disease of the respiratory tract is a fertile field for the cultivation of diagnostic axioms, and perhaps none has greater importance for the general practitioner than Dr. Cole's observation that *patients who are "threatened with" pneumonia usually have it.* This, in other words, means that the diagnosis of pneumonia does not have to depend on actual evidence of consolidation, but on the history, coupled with the presence of *any* abnormal signs in the lung. When we consider that whatever form of treatment we employ—whether serum, chemotherapy, or any other—the *earlier* treatment is started the *lower* the mortality rate, the significance of this observation becomes apparent.

Another condition which is almost always present if it is suspected, is *fluid in the chest*. Whether transudate or pus, if there is any doubt as to whether or not it is present, it usually is. *The diagnosis is made by the fingers.* A stethoscope is not necessary; nor is any instrument of precision. The cardinal signs are dulness, diminished fremitus, and displacement of organs. Any other abnormal physical findings are due to something else. In this connection, it might be appropriate to mention "*unresolved pneumonia*," a diagnosis which is being made less often than formerly, and a condition which despite claims to the contrary probably does not exist. As a rule, "*unresolved pneumonia*" is either *fluid*—pleural, encapsulated, or interlobar—or *abscess*.

Another diagnosis which is often made, but which is less common now than formerly, is "bronchitis." Conceivably there is a pathologic entity which could be called "acute bronchitis," especially in children, but if, in adults, an acute upper respiratory infection extends beyond the trachea, it becomes bronchopneumonia. "*Chronic bronchitis*" is not a disease at all, but an incident. In New England, it is usually a sequel of chronic

sinusitis and a precursor of bronchiectasis, emphysema, and, ultimately, broncho- or lobar pneumonia.

There are some other generalizations about New England upper respiratory infections which may be worth mentioning: It is common knowledge that the vast majority of patients, up to middle age at least, when they develop a "head cold"—be it coryza, pharyngitis, or laryngitis—run a course of four or five days and recover uneventfully. If the patient be past middle age, and especially if he be elderly, a "cold in the head" usually becomes an infection in the lungs. There is one notable exception to this: If such an infection starts as laryngitis, and has not some more serious underlying cause, recovery is usually prompt. But a "*head cold*" (by which we mean an acute rhinitis or coryza) *occurring in an elderly person almost always turns out to be a wrong diagnosis.*

One more truism concerning the diagnosis of pulmonary disease: *Asthma*, occurring for the first time in middle age or after, is due to *cardiac* or *renal* and not *pulmonary* causes.

**Comment and Summary.**—It has not been the purpose of this paper to do more than list a few of the diagnostic axioms applicable to one or two branches of medicine. To attempt to do more would be at once over-ambitious and futile: Over-ambitious because there is no limit to the number of maxims which might be compiled in any single field of medical diagnosis; futile, because such axioms are of necessity superficial and but scratch the surface. The practice of medicine and the art of diagnosis cannot be based on rule-of-thumb generalizations, but on the deeper knowledge from which, in turn, may evolve a few maxims of general application. An attempt has therefore been made to confine these maxims to diagnostic methods and principles, rather than to extend them to cover specific diseases.

In conclusion, it may be pertinent to call attention to two ideas, both of which have been expressed above in somewhat different fashion: The first might be called the "pitfall of statistical diagnosis." As in prognosis, when for example we know that a mortality of 50 per cent accompanies a given dis-

ease, we may be prone to come to the erroneous conclusion that for this reason, our patient with this disease has a 50-50 chance of recovery. So in diagnosis, when we meet a symptom complex that may occur in each of several diseases, we should not decide on the disease which is most common, but rather, as best we can, on the *particular features* of the individual case.

Finally and most important—because probably the physician never lived who was not at some time guilty of transgression in this respect—one more quotation from Dr. Houston must be given: *Diagnoses which are made to obtain rest from puzzling over a problem are always wrong—wrong in principle.*

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*Acknowledgment:* In preparing this paper the writer has borrowed freely from his "Medicine in the Outpatient Department" (N. Y., Hoeber, 1938), and he takes this occasion to thank Mr. Paul B. Hoeber for permission to do so.



## CLINIC OF DR. EDWARD S. EMERY, JR.

FROM THE MEDICAL CLINIC OF THE PETER BENT BRIGHAM  
HOSPITAL

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### ACUTE DISEASES OF THE DIGESTIVE SYSTEM: DIFFERENTIAL DIAGNOSIS AND TREATMENT

THERE was a time when any severe epigastric pain was thought to result from an acute disturbance of the stomach. Therefore, such a symptom was diagnosed as acute indigestion. Later, it was recognized that many of these attacks, particularly if followed by death, were the result of coronary thrombosis; and today, "*acute indigestion*" is associated in the minds of most physicians with an acute cardiac condition. For the purpose of this clinic, however, the term "*acute indigestion*" will be used in its original sense; as a sudden, severe pain occurring in the epigastrium from any cause.

#### CASE I

This patient who is being presented has suffered from just such a symptom (outline of history presented by medical student):

*History.*—The patient is a forty-eight-year-old married, white female, with two children, who entered the surgical service February 25 with a complaint of epigastric pain for three days and nausea and vomiting for two days.

Her *past history* is interesting in that, twenty years ago, she suffered from epigastric distress which was relieved with food and soda. In 1922 she was seen in the out-patient department for the same complaint, at which time x-rays were advised but were not taken. In 1927, while cooking at home, she had a sudden pain in the epigastrium, felt weak and went to bed. She had profuse sweating and vomited some coffee-ground material and the next day passed several loose, coal-black stools. On entry to the surgical service x-rays of the gastro-intestinal tract showed a duodenal ulcer and cholecystograms were



said to show gallstones. Since 1927, she has not been bothered by stomach symptoms. For the last ten years she has noticed palpitation on exertion. Nine years ago, during an attack of acute bronchitis, she had one attack at night, when she had to get up and sit by an open window because she felt stifled. She has had about five attacks since then. For the last year and a half she has had attacks of pain over the precordium; this pain usually starts a little bit to the right, radiates to the left and, later, to the inside of the right arm and sometimes to the left arm. These attacks are usually brought on by exertion, but sometimes they come on with nervousness or emotion.

The *present illness* started three days ago when the patient was at a theater and was suddenly seized with an acute stabbing pain in the epigastrium which radiated through to the back. She rested for an hour after the movies were over and then was able to go home and walked up three flights of stairs. The next day she vomited every three or four hours a bile-stained material with no blood.

The *essential finding* on her entry to the hospital was rather severe epigastric tenderness but no spasm. The heart was enlarged and her blood pressure was 180 systolic and 100 diastolic. Because of some dehydration she was given 1500 cc. of saline subcutaneously. Intravenous cholecystograms showed a normal gallbladder. Because no acute surgical condition was indicated, the patient was transferred to the medical service.

In summary, then, we have here a forty-eight-year-old housewife with a past history of peptic ulcer for twenty years; palpitation and dyspnea on exertion for ten years, and "anginal attacks" for one and a half years, who entered the surgical service with severe epigastric pain associated with nausea and vomiting for three days.

**Findings on Examination.**—As you can see, the patient is a somewhat obese and florid individual who at present is lying comfortably in bed on one pillow. The *lungs* are resonant and their examination is essentially negative. By percussion, the *heart* is perhaps slightly enlarged to the left. The sounds are of good quality. A rough, somewhat faint systolic murmur is heard over the base and to the left of the sternum. The *arteries* are not thickened and the *eyegrounds* do not reveal any recognizable vascular changes. The *blood pressure*, which was 180/100 on admission, is now 155/95, a drop which can be readily explained on her rest in bed. These findings are, therefore, compatible with some roughening of the aortic valve and confirm the idea that this patient has been suffering from cardiac symptoms.

At the present time, the *abdomen* is soft and easily examined throughout. Except for a palpable liver edge one finger's breadth below the costal margin, no masses are felt. Upon asking the patient to raise her head, there is no evidence of any abdominal herniation. The *temperature* chart shows that there has been a fever of 101° F. only once, and that was shortly after admission to the surgical service. The *pulse* and *respiration* have remained continuously around 80 and 20, respectively. The *blood* has been normal at all times, with a hemoglobin of 90 per cent, red cells 5,300,000, and white cells which never have been above 12,000 per cu. mm. and have gone as low as 5000. The blood smear has been entirely normal except for an eosinophilia of 5 per cent. Blood Wassermann and Hinton tests are negative. The *urine* showed the slightest possible trace of albumin and one white blood cell. A phenolsulfonphthalein test showed 60 per cent excretion, which is normal for the method used. An *electrocardiogram* showed left axis deviation and a normal fourth lead. A *roentgenogram of the chest* showed the lungs to be clear. The heart is prominent downward and to the left. It is not measurably enlarged. *Gastric analysis* shows 40 units of free hydrochloric acid. *Stools* have shown a 1 to 2 plus guaiac.

**Differential Diagnosis.**—First of all we have no evidence that this patient has an acute surgical condition. She did not have a board-like abdomen which comes from involuntary spasm and, in fact, there was no muscular spasm a few hours after the onset. There was no indication of peritoneal irritation as shown by the absence of rebound tenderness. With an essentially normal temperature and no significant leukocytosis, we do not have to think of an acute infection. Therefore, we can eliminate a *free perforation into the abdominal cavity*.

Acute epigastric distress such as this patient has had may come from many causes: *i. e.*, from diseases of the *esophagus*, *heart*, *stomach* and *duodenum*, *liver* and *gallbladder*, *pancreas*, *diaphragm*, *appendix* and *kidney*, *herniation of the linea alba*, *tabetic crisis*, *lead colic*, *dissecting aneurysm of the aorta*, and

*embolism.* The commonest causes are diseases of the heart, peptic ulcer, an acute gallbladder, acute pancreatitis and, more rarely, an acute appendix. In this particular case we can quickly eliminate the esophagus by the absence of typical esophageal symptoms. The physical examination rules out herniation through the abdominal wall. The history and laboratory studies seem to effectively dispose of tabetic crises, lead colic, the kidneys and the gallbladder as a cause of this woman's trouble.

Let us therefore consider the two conditions which this patient has apparently suffered from in the past and which can produce severe epigastric pain; namely *heart disease* and *peptic ulcer*. There are three cardiac conditions which can produce severe epigastric pain: angina pectoris, coronary occlusion, and acute pericarditis. The past history suggests that this patient has suffered from *anginal* symptoms. If we had seen her during the attack we should undoubtedly have had to seriously consider angina as a definite possibility. With our present knowledge there are certain reasons to doubt this. Her previous anginal attacks had never involved the epigastrium. After the attack was over she was able to go home and climb several flights of stairs without a recurrence of distress. One would expect that this amount of exertion would bring a return of symptoms if she had so recently recovered from an attack of coronary spasm lasting three hours. It is unusual for an attack of abdominal angina to be followed by a prolonged period of nausea and vomiting. Finally, epigastric angina does not radiate directly through to the back. If we had seen her during the acute distress, we would certainly have been thinking of a coronary occlusion. But we know now that she has not shown at any time the characteristic findings of collapse, a marked drop in blood pressure, the leukocytosis and the electrocardiographic changes which we expect to accompany an occlusion. Therefore it seems justifiable to eliminate this condition.

Again, we have no evidence for an *acute pericarditis*. No one has heard a pericardial friction rub, which is the surest

sign that such a condition is present. However, this is often transitory or faint and may be missed. It could easily have disappeared before the patient's entry into the hospital. The absence of fever, the failure to develop pericardial fluid and the brevity of the attack, leaves no data on which to diagnose such a condition. Therefore, although we had every reason to suspect a cardiac cause of this woman's pain when she was first seen, it appears now that some other factor was responsible.

Turning to the possibility of *peptic ulcer* which she is known to have had, we can find several points compatible with it: Although it is somewhat unusual for an ulcer to come on so abruptly and so intensely without any premonitory symptoms, it can happen. The pain was referred directly to the back, which suggests involvement of the posterior abdominal wall. Whenever a patient complains of pain in the back associated with abdominal pain, it is well to remember that spinal disease may be responsible even though the patient is convinced that the pain originated in the abdomen. In this case, however, there is no evidence for spinal disease and it can be ruled out. This pain is compatible with a penetrating ulcer which has involved the posterior abdominal wall and the nausea and vomiting goes with it. The fact that the original attack has not been followed by further ulcer symptoms would tend to place it in the stomach rather than the duodenum because a duodenal ulcer is much more likely to continue giving distress. Clinically, we will therefore have to consider seriously a peptic ulcer until an x-ray of the stomach confirms or eliminates this possibility.

We must think also of *other gastric conditions* which may produce acute epigastric distress: An *acute gastritis* may do it, but there is no history of the patient having taken any incriminating food or drink and an acute gastritis is not likely to refer pain to the back. A *herniation of the stomach* through an esophageal hiatus of the diaphragm can produce acute pain even with bleeding. It can also cause substernal discomfort and a sense of suffocation, particularly at night, such as this

patient had had in the past. But these complaints are not brought on by emotional factors and exercise such as this patient has experienced. It is something that we are not in a position to rule out entirely at the moment, but I should place it secondarily to the possibility of an ulcer. Also, the *x-ray* examination will be useful in determining the presence or absence of this condition. However, we should tell the roentgenologist that we are *considering a herniation* because it is very easy to miss by the *x-ray* if one is not looking for it. In fact, a herniation sometimes will not show when one is definitely expecting it.

There is a difference of opinion about the possibility of *duodenal diverticula* producing chronic symptoms. However, they can produce acute symptoms mechanically. This is sometimes not fully appreciated because the diagnosis has to be made by the *x-ray*. These diverticula may also be difficult for the roentgenologist to observe, particularly if they are located in the duodenojejunal flexure which is covered so often by the stomach. Hence, many of these diverticula have been missed. However, there is nothing about this case which causes us to entertain seriously the idea of a duodenal diverticulum.

The cholecystograms done on the surgical service before we saw this patient adequately ruled out the *gallbladder* as a source of trouble. Otherwise, we should have to take this possibility into consideration. Acute epigastric pain referred to the back and leaving soreness in its wake is entirely compatible with a biliary disturbance. Moreover, gallbladders can refer pain to the substernal region and suggest a cardiac condition just as the reverse is true. It is to be remembered that the vagus nerves supply the heart and all of the upper abdominal viscera and pain can be referred in either direction. Although the typical points of reference from biliary distress is straight through to the back and the tip of the right shoulder, we occasionally find pain referred to unusual places. However, this patient's substernal discomfort was brought on by exertion and emotion in a way which does not precipitate gallblad-

der distress, so that even if she had been found to have a pathologic gallbladder, we would still diagnose angina.

Acute or subacute *pancreatitis* is another cause of epigastric pain. Located on the posterior wall of the epigastrium, an inflamed pancreas can easily produce epigastric distress with tenderness and pain radiating to the back. This important organ has not received the attention it should because we had developed no easy diagnostic procedures before Wohlgemuth described his modified diastase test. Therefore, we have been limited to diagnosing only the acute fulminating disturbances. Yet postmortem studies reveal fibrous changes which may represent inflammatory disorders that were undiagnosed during life. And more recently, it has been reported that frequent diastase tests will reveal a pancreatitis in otherwise unexplained cases of chronic indigestion. It is possible that further experience with and a greater use of the diastase test will reveal the need for using it as freely as cholecystograms. It seems reasonable to suppose that the pancreas may suffer from chronic inflammatory disease and be responsible for as much epigastric trouble as the gallbladder. A diastase test has not been done on this patient and we have no evidence on which to base a diagnosis of subacute pancreatitis. Certainly the patient did not have the collapse, cyanosis and boardlike abdomen characteristic of an acute pancreatitis.

*Emboli* can produce pain anywhere in the abdomen and give physical signs which vary greatly in their intensity depending upon the extensiveness of the process. I recall a patient in which the medical and surgical consultants could not agree on whether the epigastric pain was a surgical or medical complication of his ulcer, when the true cause of the trouble was multiple emboli from a fibrillating heart. In this case, however, there is no known source for emboli and I think they can be dismissed.

Finally, we should give some thought to the *eosinophilia*. I have seen one patient who was explored for intestinal obstruction because of symptoms which were the result of an acute allergy. Therefore, it is well to keep in mind that gastro-

intestinal allergy may produce alarming symptoms. However, this patient gives no history suggestive of an allergic tendency.

**Diagnosis.**—In conclusion, we can say that with our present clinical knowledge this patient suffers from angina pectoris and that she has had an acute gastro-intestinal disturbance, the cause of which is an acutely penetrating peptic ulcer, although the possibility of a diaphragmatic hernia should be considered. *x*-Ray studies of the gastro-intestinal tract reveal a large penetrating gastric ulcer located at the junction of the middle and distal thirds of the stomach and presumably involving the posterior abdominal wall.

**Final Diagnosis:** Penetrating gastric ulcer, angina pectoris, chronic hypertensive vascular disease.

## CASE II

This next patient is a twenty-five-year-old man who entered the hospital with the complaint of *abdominal pain* and *vomiting*:

**History.**—This patient had always considered himself essentially well, except that, eleven months ago, he had an attack of rather acute and severe pharyngitis. He has been working very hard for the past nine months; has been feeling quite tired of late and thinks he has lost some weight. During the past few months he has noticed a sensation of epigastric fullness after a large meal which he has attributed to fatigue and states that he has not had any more indigestion than a normal person might reasonably expect.

The day before admission he felt perfectly well and, during the evening, ate a heavy meal. About midnight he began to feel nauseated and vomited a considerable quantity of fluid mixed with some of the food which he had recently taken. Shortly after this, he was seized with an extremely severe pain in the mid-epigastrium. He lay curled up on a couch for three hours in considerable agony, being most comfortable when doubled up and with his hand pressed against the upper abdomen. Toward morning the pain abated somewhat and, about 8:30, he was able to walk across the street and eat a light breakfast, but he vomited this very soon afterward. He was then brought to the hospital where he was seen about 10 A. M.—at which time he stated that the pain was more severe in the left upper quadrant directly below the costal margin.

**Findings on Examination.**—Physical examination at this time revealed a flushed face and the patient was obviously

in great distress. The abdomen was spastic throughout the upper half and the maximum point of tenderness coincided with the pain under the left costal margin. There was no tenderness or spasm in the umbilical region or the lower abdomen. The rest of the physical examination was essentially negative. He had a normal temperature and a normal white count. Because he stated that the pain was becoming less marked, and in view of the recent dietary indiscretion, it was decided to give him a small amount of codeine and await developments. By early afternoon he felt well enough to eat a small amount of ice cream, but he did not relish it and soon vomited again. Toward the latter part of the afternoon, the upper abdomen was still tender and spastic and he now had a leukocytosis of 15,000. He was given an enema, with no results, and a hypodermic injection of  $\frac{1}{4}$  grain of morphine. By 3:30 A. M., when the effect of the morphine had worn off, he was in extreme agony and his lower abdomen had become spastic. His white blood count at this time was 15,000; the temperature was 102.2° F., the pulse 90, strong and regular. It was then decided to wait no longer and he was immediately explored.

**Differential Diagnosis.**—In going back over this patient's history, we find that the first symptoms of which he complained were some nausea and vomiting. The *causes of vomiting* are numerous:

1. Local irritation of the stomach or intestine as a result of excessive eating or drinking, infection and allergy.
2. Obstruction from any one of many causes.
3. Toxic causes, such as occur in nephritis.
4. Reflex disturbances which may develop for a number of reasons, such as pain, disease of the middle ear, peritonitis, renal disorders, etc.
5. Diseases of the central nervous system, such as brain tumor, meningitis, tabes.
6. Glandular disorders, as in the case of vomiting of pregnancy.
7. Functional vomiting, as occurs in hysteria.



In this case, there are several possibilities that should be considered. Irritation, obstruction and a reflex cause such as pain or peritonitis must be kept in mind. The sudden onset of severe pain with marked spasm, of course, suggests an acute surgical condition of some kind and one would immediately think of a *perforation*, an *acutely diseased gallbladder*, *acute pancreatitis*, an *intestinal obstruction*, and a *mesenteric thrombosis*. However, the presenting symptoms of severe pain with somewhat localized tenderness and marked spasm tells us only that he has an irritation of the peritoneum. There was no evidence of infection at the time of entry as shown by the normal temperature and white count. The fact that this episode followed within a few hours of an unusually large meal suggests the possibility that the patient might have suffered from an *acute gastritis* so that it was felt justifiable to wait for a period of time to observe developments.

As his condition continued to get worse rather than better, however, and he began to show evidences of developing an infection, it became obvious that he was suffering from a serious condition. An acutely *penetrating ulcer* is a common cause of severe epigastric pain without signs of spasm, such as this case presented. However, one would feel better about making such a diagnosis if there had been a previous history suggestive of this disease. The fact that the pain was on the left side somewhat eliminated this possibility, although a patient whose ulcer has perforated may experience pain on the left side, but it is more commonly in the midline or slightly to the right. The fact that the pain tended to subside would mean that if an ulcer had perforated, it must be a small perforation which had been partially walled off by the omentum and that small leaks occurred from time to time. A wide open perforation would have produced continuous pain. Although any severe upper abdominal distress should suggest gallbladder disease, the location in the left upper quadrant rather than on the right side is definitely opposed to this diagnosis, particularly as the maximum point of tenderness was also on the left side.

Vomiting is a very common accompaniment of *pancreatic disease*. Also, it is of interest that in the early stages of acute pancreatitis there is frequently no evidence of infection.

You notice that when this patient was first seen, ten hours after the onset, he showed no fever or leukocytosis. By afternoon, his white count had risen to 15,000. At the end of twenty-four hours he had a fever of 102.2° F. and his white count was still 15,000. This lag in the development of a leukocytosis and fever is also characteristic of an acutely diseased pancreas. Also, just as in this patient, the leukocytosis tends to develop before the fever. Intestinal obstruction and mesenteric thrombosis should be considered. However, there is nothing in the patient's history to suggest intestinal obstruction other than pain and vomiting and it is doubtful if the patient would desire to eat if such a condition exists.

It is conceivable that a *mesenteric thrombosis* could give these symptoms, but the location of pain would place it high in the intestinal tract, which is somewhat unusual, and it is also unusual for this condition to occur in as young a patient as this man.

**Diagnosis.**—In summary, therefore, it appears that *everything points to the pancreas*, which was found to be the case at the time of operation. The gland as seen through a rather thin gastrohepatic omentum did not look normal as a whole. An opening was made just below the stomach through which one finger was passed and the surgeon got the impression that the pancreas felt abnormal, giving a slightly elastic sensation. However, if it had not been for some blood-tinged fluid and the pressure of some fat necrosis, the operator could not have said that it was an acute pancreatitis. Because of these findings, a drain was put in the wound and the incision closed. The patient made a rapid recovery and, as you can see, looks and feels very well. This is a classical picture of acute pancreatic edema as described by Zoepfell.

*Acute pancreatic necrosis* gives more severe symptoms than this patient presented. *Suppurative pancreatitis* usually pre-

sents a higher white count, sometimes reaching 30,000, and ultimately produces a septic type of temperature.

About half of the patients with acute pancreatic disease show a hyperglycemia in the fasting blood sugar. An increase in urobilinogen has also been reported by some writers. Others have found, in the early stages, a blood lipase capable of splitting olive oil. The most useful laboratory procedure is the *modified diastase test of Wohlgemuth*, which gives a high reading within the first twenty-four hours after onset but usually drops to normal quite rapidly after this. As a reading can be made within an hour, any well-equipped laboratory should be prepared to perform this test.

This patient was operated upon because we were not sure of the diagnosis. If it had been known that he had an acute pancreatitis this would not have been attempted. It is now generally realized that this condition can be treated better medically than surgically. The patient should be made comfortable with a sufficient amount of morphine, and fluids must be kept up by intravenous injections of glucose. This method of treatment reduces the mortality about 50 per cent of what it used to be with surgery.

### CASE III

The next patient was first seen by me four years ago, at which time he came for a general physical examination:

**History.**—This patient had been feeling somewhat tired and was worried about the possibility that his appendix might be diseased. He is now thirty-two years old and has been troubled with mild dyspeptic symptoms for a number of years. Two years before I saw him he had been told that he might have some trouble with his appendix. Examination at that time was essentially negative except for his ptotic build which you can see today. He was always somewhat underweight and finds that he tires quite easily. During the last two or three years he has consulted me on numerous occasions about a slight dragging sensation in the right lower quadrant. A year and a half ago he stated that this discomfort was becoming more troublesome and he noticed it particularly after playing badminton or taking other violent exercise. It has been located just above Poupart's ligament and he can reproduce it by leaning backwards in such a way as to stretch the abdominal muscles.

On the various occasions that he has consulted me he has never shown any tenderness or leukocytosis. The story of the present attacks is as follows:

He called me at four o'clock on the day he entered the hospital because of what he first described as summer complaint, but on further questioning it developed that he had begun to suffer from a stomach ache at noon time. He had had a bowel movement which did not relieve the distress. He was about to start for a neighboring town and wished to know what he could do for his trouble when he reached home. The discomfort was not severe and it was only after considerable urging that he agreed to see me in my office. This he did at 4:30 in the afternoon, and stated that he still had a little discomfort and on direct questioning I elicited the fact that it had moved from the mid-epigastrium somewhat toward the right lower quadrant.

**Findings on Examination.**—Physical examination at this time was essentially negative. There was no spasm and only questionable tenderness in the region of McBurney's point. Certainly this was no more than we frequently find in patients on a routine examination. Furthermore, a rectal examination was entirely negative. However, the patient did have a slight fever of  $99.7^{\circ}$  F. and a white blood count of 18,000. Therefore I advised him to see a surgeon, who believed that it was extremely unlikely that he had appendicitis, but who because of the leukocytosis advised him to remain in the hospital overnight. At nine o'clock his white count had reached 22,000 and the surgeon operated immediately, at which time a very acutely inflamed and distended appendix was removed.

**Differential Diagnosis.**—I am showing this patient to illustrate the importance of the *tenderness* and the *white count* in a suspected case of appendicitis. This represents the sort of situation in which the physician so often has to make a decision. We commonly see individuals who are troubled with discomfort in the right lower quadrant and in whom it is frequently possible to elicit some tenderness over the region of the cecum. Ordinarily, mild tenderness in this area does not have much significance. Many patients with *functional* distress and suffering from the so-called irritable colon will experience varying degrees of tenderness in this region. In fact, patients normally experience more tenderness in this area than in the other portions of the lower abdomen. Many functional

cases complain of so much trouble that the diagnosis of chronic appendicitis is frequently made and many appendicectomies have been done without any relief.

This patient has complained of discomfort in his right lower quadrant for a long time, although he has never had an attack similar to this. It will be interesting to observe whether the removal of his appendix is going to relieve him of the symptoms which he has been having. In my experience, we have no way of knowing. It is possible, I suppose, that his former symptoms have been due to some trouble with his appendix. On the other hand, there has been nothing about them that differs from patients with functional disorders. Furthermore, we know he is viscerotonic, and individuals of this type are more likely to suffer from functional disorders than the sthenic type. This patient presented nothing on physical examination to suggest acute appendicitis. He, himself, believed that he was having an ordinary attack of indigestion and, in fact, this was the one time that he did not believe he had appendicitis. As already stated, the surgeon was very doubtful about it. It would have been easy to have reassured this patient and sent him home without bothering to take his temperature or to do a white count. I must admit that it seemed a little unnecessary when I saw him. However, after seeing the appendix when it was taken out, it seems improbable that it would have gone through the night without perforating.

Acute appendicitis is one of the acute diseases of the digestive system, the diagnosis of which may be the simplest thing in the world. However, this case illustrates that it is possible for an acute appendix to produce symptoms which are no different or no more severe than many functional conditions. The temperature and white count may be the deciding factors. Oftentimes, it seems unnecessary to bother with these procedures, but it is the only way that a physician can be sure that he is not missing an acute inflammation. This case also illustrates how impossible it may be for a consultant to decide whether a patient suffers from attacks of appendicitis on the basis of the history. The diagnosis has to be made *at the*

*time the patient is experiencing symptoms.* In the great majority of instances, it is the family physician who will have to make the diagnosis.

Finally, these cases illustrate another point: A patient who is having pain and tenderness in the right lower quadrant and who has a fever and leukocytosis should be considered to have an acute appendix *if no other cause for his symptoms can be found.* There are numerous reports in the literature that the mortality from appendicitis is as great, in fact greater than it used to be. One way by which this mortality can be decreased is a greater use of the laboratory procedures in suspected or suggestive cases of appendicitis.



## CLINIC OF DR. DONALD S. KING

### MASSACHUSETTS GENERAL HOSPITAL

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#### ACUTE DISEASES OF THE RESPIRATORY SYSTEM: DIFFERENTIAL DIAGNOSIS OF THE PNEUMONIAS AND OTHER COMMON ACUTE PULMONARY CONDI- TIONS

I SHALL present today a group of cases illustrating the common types of acute pulmonary conditions, including the various *pneumonias*, *tuberculosis*, *abscess*, *postoperative atelectasis* and *infarction*.

The symptoms to be considered particularly are *chill*; *fever*; *pleural pain*; *cough*; and *bloody, rusty, or purulent expectoration*. The *differential diagnosis* will be based on an evaluation of these plus physical signs, laboratory studies of sputum and blood, and usually the chest x-ray film. After discussing the diagnosis I shall in most cases indicate the main line of treatment:

**Case I. Lobar Pneumonia (Type II Pneumococcus).**  
—Mrs. M. W. is thirty-three years old. Eight years ago she was studied because of sterility, and a pelvic operation was performed. At the onset of the present illness she was in the third month of her first pregnancy and there had been persistent urinary frequency. On the day before her admission to the hospital she developed severe pain over the left lower chest which was aggravated by breathing. There were recurrent chills. Examination of her lungs gave no definitely abnormal signs, and because of the pregnancy and urinary symptoms pyelitis was suspected. In the evening, however,



there was cough and bloody expectoration. She was admitted thirty hours after the onset. The temperature by rectum was 102.4° F. with a rise to 104° within three hours; the pulse was 155 and respirations 48. There was bronchial breathing in the left lower back and a few râles. During the examination sticky rusty sputum was expectorated. The white cell count was 29,500, and a portable x-ray showed consolidation of the left lower lobe.

The sudden onset with chills, pleural pain, high fever, rapid respiration and rusty sputum made the diagnosis of pneumococcus lobar pneumonia almost certain. The only atypical symptom was the *recurrence* of chills. A single severe chill is more characteristic of pneumonia due to pneumococcus, particularly Types I and II, and the recurrence here may have been of chilliness and not true chill. In any case, immediate Neufeld examination of the sputum showed Type II pneumococcus. Fortunately all the studies so far reported were completed within an hour and a half after admission and early treatment could be planned. The patient was seriously ill with a very rapid pulse, and it is well known that pregnancy increases the gravity of prognosis in any case of pneumonia. Besides this the pregnancy was the first in more than eight years of marriage and everything possible had to be done to prevent miscarriage. We therefore decided to give the *combined sulfapyridine and serum treatment*, and 200,000 units of Type II rabbit serum were injected.

The following morning the temperature was still 102.4° F. rectally. The patient had had 5 gm. of sulfapyridine in addition to the rabbit serum and we were disappointed that there had not been a more marked temperature drop after sixteen hours of treatment. Three questions presented themselves: (1) Was it possible that there were two types of pneumococcus to combat; (2) should more Type II serum be given; and (3) should sulfapyridine be discontinued. Sputum was again sent to the laboratory, but no other types of pneumococcus could be found. The intradermal Francis test<sup>1, 2</sup> using Type II pneumococcus carbohydrate had been made before the

serum was given and was negative. This test was now repeated and a 13 mm. urticarial wheal with pseudopods appeared within twenty minutes. We took this to mean that sufficient serum had been administered and decided to continue sulfapyridine. By seven o'clock in the evening, the temperature had dropped to 99° F. by rectum and sulfapyridine was discontinued because of nausea and vomiting. The next day the temperature rose to 100° F., but was never higher than that and no more drug or serum was given. Unfortunately the patient miscarried nine days after admission.

I have presented here a typical case of *lobar pneumonia*, caused by Type II pneumococcus. The patient was severely ill and there was the complication of pregnancy. The treatment of combined serum and sulfapyridine was effective in curing the pneumonia but miscarriage could not be prevented.

**Case II. Primary Atypical Pneumococcus Pneumonia.**—Mrs. M. D., aged forty-one, developed symptoms said to be due to "grippe." At the onset the oral temperature was 100.4° F. and the pulse 90. She was not seen again by her local physician until five days later, at which time she had pain in the left upper chest and râles were heard in this area. During the next five days her temperature varied from 100° to 104° F., the pulse was 110 to 125 and of poor quality, and the respirations 40. She had severe chills but no bloody or rusty sputum. Cyanosis was marked, and at times she was irrational. She was digitalized and given coramine and caffeine.

I saw the patient in consultation ten days after the onset. She was then markedly cyanotic and irrational, the abdomen was distended, and there were signs of consolidation in the right upper and left lower lobes. Type XXV pneumococcus was found in the sputum, and the prognosis seemed poor. Rabbit serum was not available for this type at the time, and it would have been rather late in the disease to expect good serum results in any case. Sulfapyridine, however, was begun immediately in addition to oxygen treatment. The tempera-

ture dropped to normal within twenty-four hours, but in spite of continuation of sulfapyridine it rose again in three days and was not normal until three days later. The patient eventually made a good recovery.

Here is a case of pneumonia probably caused by one of the "higher types" of pneumococcus with a slow onset of serious illness, no bloody or rusty sputum, and an up-and-down temperature. A few years ago this would have been classified as severe "confluent bronchopneumonia." Since there was no evidence of an underlying disease to which the pneumonia was secondary, perhaps the best classification is "primary atypical pneumococcus pneumonia" (Reimann).<sup>8</sup> In such cases it is not worth while to spend time trying to determine whether there is broncho- or lobar pneumonia, but rather to make every effort to identify the etiologic organism and treat on a bacteriologic, not anatomic, basis. The problem is not easy, for the type of pneumococcus involved is almost always one that is commonly present in the mouth of a healthy person, and unless it is found on repeated sputum typing, by blood culture, lung puncture, or in the pleural fluid, it is difficult to be sure that it is causing the disease. Type XXV pneumococcus is one of the rarer types, and so few cases caused by it are reported in the literature that we have no real information as to its mortality rate. At present, however, if a patient with a similar infection did not improve with sulfapyridine, rabbit serum would probably be given even as late as ten days after the onset of the illness.

**Case III. Virus Pneumonia.**—Miss E. Z., aged thirty-five, had a severe headache followed the next day by general malaise and aching through the arms and legs. Two days after the onset there was a series of chills, with a hacking cough and pain beneath the xiphoid aggravated by breathing. Breath sounds at the left base were diminished. The white count was 12,200 with 84 per cent polymorphonuclears. She was admitted to the hospital and the x-ray showed an area of consolidation in the left lower lobe. Repeated white counts

ran from 8,000 to 11,000. There was a very irregular temperature, ranging from 98° to 103° F. by mouth, pulse was 90 to 110, and respirations 25 to 35. On the seventh day of the disease there was a severe chill, lasting thirty minutes, and the following day another chill. She had dyspnea and cyanosis. x-Rays showed a spread of the process in the left lower lobe and a new area in the right upper. No sputum could be obtained for examination, and throat culture showed no pneumococci or hemolytic streptococci. Blood cultures were repeatedly negative. Sulfapyridine was tried, but vomiting was so severe that it had to be discontinued. (The gastric symptoms were due in part to an acute duodenal ulcer.)

Two weeks after the onset of symptoms, a Type II pneumococcus was recovered from a mouse which died three days after it was injected with sputum, but it is very doubtful if this finding was of etiologic significance. The picket-fence temperature persisted for seventeen days from the onset, when it dropped to normal in two days' time.

In this case we are considering a prostrated pneumonia patient with a picket-fence temperature lasting more than two weeks, hard dry cough, dyspnea and cyanosis, a normal white count and no obtainable evidence of an etiologic organism. Clinically the description is similar to that reported of cases in which a virus has been demonstrated,<sup>4</sup> but no attempt was made here to find one. If a virus was present, it was probably not that of the common cold or of influenza (infection which usually gives a true leukopenia)<sup>5</sup> but one of the group as yet unidentified. Sulfapyridine is seemingly of no use in this type of infection.

Some cases like this one have after several days of running a low white count suddenly developed a very high one and hemolytic streptococcus empyema, but there is no proof that they are primary hemolytic streptococcus pneumonias.

**Case IV. Primary Hemolytic Streptococcal Pneumonia.**—Mr. R. B., fifty-four years old, developed cough and greenish yellow expectoration two weeks before his admission

to the hospital. A week after the onset there were alternating periods of chilliness and fever with drenching sweats, diarrhea, dyspnea and a sense of constriction across the chest. On admission the temperature was 100.6° F., pulse 100 and respirations 44. There was prostration, rapid respiration, marked cyanosis and moderate jaundice. Physical examination showed *musical râles throughout the chest and moist râles at both bases*. The liver edge could be easily felt. Sputum was mucopurulent, not rusty or bloody, and on culture showed numerous colonies of hemolytic streptococci. Blood cultures taken on admission were negative. Tests for typhoid and undulant fever were negative. The x-ray film showed mottling throughout both lungs and was interpreted as receding pneumonia, possibly miliary tuberculosis.

On admission, the white count was 12,000 and rose steadily to 75,000. The red count fell from 4,400,000 to 1,700,000, and the hemoglobin from 62 to 48 per cent. Two transfusions were given, but the patient died twenty-four days after admission. Autopsy showed bilateral bronchopneumonia, empyema in the left thoracic cavity and generalized arteriosclerosis. Cultures from the heart's blood and the pleural fluid showed hemolytic streptococcus.

This is probably a case of primary hemolytic streptococcus pneumonia, though we cannot be sure that there was not some other initial invader. The one element lacking to make it typical of streptococcus pneumonia is a story of early throat infection. Unfortunately this case occurred before the days of sulfanilamide.

**Case V. Secondary Bronchopneumonia.**—Mr. T. H. was seventy-four years old when he began to have recurrent "winter bronchitis." Six months before his entry he had dyspnea on exertion, edema of the ankles and urinary urgency. Three days before his admission to the hospital, and four days before his death, he developed a tickling sensation in his throat and a dry hacking cough with substernal pain. Dyspnea became more marked with later orthopnea. There were no chills

and no known fever, but there was excessive perspiration. On admission the temperature was  $101^{\circ}$  to  $102.5^{\circ}$  F. There were many moist râles over the bases of the lungs. The heart was enlarged to the left and a loud systolic murmur could be heard at the apex. Blood pressure was 130/90. The abdomen was distended. No sputum could be obtained for examination. On the day after admission the patient died.

Postmortem examination showed bronchopneumonia in both upper lobes. Besides this there was generalized arteriosclerosis, including the coronary arteries, a calcareous aortic valve, cardiac hypertrophy, chronic congestion of lungs and liver, bilateral hydrothorax and chronic vascular nephritis. This is an instance of terminal bronchopneumonia of unknown etiology secondary to generalized arteriosclerosis with cardiovascular disease and congestive failure. There was, of course, little that could be done by way of treatment for the pulmonary condition.

**Case VI. Atypical Pneumonia of the Adolescent.**—Miss A. M., aged eighteen, a college freshman, was admitted to the infirmary with general malaise and an oral temperature of  $101^{\circ}$  F. The following day the temperature was normal but, on the third day, it had returned to  $101^{\circ}$  F. and she had headache and reddening of the pharynx. The white count on admission was 7,600. On the tenth day the temperature was still  $101.4^{\circ}$  F. Mucopurulent sputum contained no typable pneumococcus and no hemolytic streptococcus. x-Ray at this time showed a bronchopneumonic process involving the right upper lobe. No cavity was present, but the picture was consistent with pulmonary tuberculosis. Three sputum specimens were concentrated, but no tubercle bacilli were found. On the twelfth day the temperature returned to normal and an x-ray film, taken one week after the first, showed the lung to be entirely clear.

Cases like this are frequently seen in boarding schools and colleges.<sup>6, 7</sup> There is obvious pneumonia present, as shown in the x-ray film, but mild or only moderate symptoms. The

temperature is up and down and the pulse rate is slower than would be expected. The white count is usually low and a typable pneumococcus or hemolytic streptococcus is rarely found in the sputum or on throat culture. The physical signs are commonly late in appearing, although occasionally there are early signs of a large area of consolidation with only mild symptoms of pneumonia. The x-ray picture is that of bronchopneumonia or a fan-shaped lesion spreading from the hilum.

Recently there has been much discussion concerning the classification of such cases. Because of failure to demonstrate the etiologic organism, some writers maintain that these mild cases, as well as the seriously ill ones, like Case III, should be called "virus pneumonia," but until the actual virus is demonstrated such a classification does not seem justified. French writers, beginning with Woillez<sup>8</sup> in 1848, have described a similar disease, stressing the fact that the alveolar exudate differs from that of true pneumonia in that it is low in fibrin content and therefore resolves rapidly. Because of the mildness of symptoms and rapid resolution of the process, many authors in this country speak of this infection as "pneumonitis";<sup>9</sup> others point to the linear markings in the x-ray film as evidence that the process is essentially interstitial and use the term "acute interstitial pneumonitis."<sup>10</sup> In our opinion the safest way to speak of this infection is as "atypical pneumonia of the adolescent and young adult."

**Case VII. Tuberculous Bronchopneumonia.**—Miss H. M., aged sixteen, had no family history of tuberculosis and no known exposure to the disease. She had always been well until she developed what was thought to be an ordinary upper respiratory infection, soon followed by pleural pain in the upper anterior part of the left chest. In the morning there was usually a slight wheeze, and a small amount of purulent sputum was raised. After a few days of illness the family physician found dulness and râles at the left apex in front. In the morning the temperature was normal but by afternoon it was

about 99.4° F. The pulse ranged between 100 and 120. The white count was 9,100, with 78 per cent polymorphonuclears, 11 per cent lymphocytes, 7 per cent mononuclears and 4 per cent eosinophils.

An alert family physician, impressed by signs of an upper lobe infection, made the diagnosis in this case by examining the sputum for tubercle bacilli. Except for the lower temperature, the case is much like the previous one, but sputum examination showed tubercle bacilli and an x-ray film taken after this finding was reported showed a typical tuberculous bronchopneumonia in the left upper lobe with a thin-walled cavity 2.0 cm. in diameter. More than a year after the disease was diagnosed in this girl, an aunt who had often driven her to school was found to have had active tuberculosis for a long time.

I shall make more comments about tuberculosis after we have considered the next case.

**Case VIII. Primary Tuberculous Pleurisy.**—Miss B. T., aged eighteen, had had scarlet fever at the age of twelve but had otherwise been well. There was no family history of tuberculosis and no known exposure. Without previous symptoms she felt, one morning, as if she were coming down with a cold and later ached all over. That evening she had a shaking chill and her temperature rose to 104° F., but there was no pleural pain and no cough. She later developed definite pleural pain and dry cough, and a temporary diagnosis of pneumonia was made. A week later, however, she had signs of fluid and 36 ounces of clear yellow fluid were removed from the pleural cavity. The afternoon temperature persisted for six weeks. A tuberculin test with a 1:10,000 dilution of old tuberculin was moderately positive. Guinea-pig inoculation of the pleural fluid showed the presence of tubercle bacilli. Repeated x-ray examination failed to show evidence of pulmonary tuberculosis.

We have here a case of primary tuberculous pleurisy with chill and a temperature of 104° F. as the initial symptoms. It was only natural to suspect pneumonia at that stage.



Case VII shows how easily a mild tuberculous bronchopneumonia can be confused with an atypical upper lobe non-tuberculous pneumonia. Case VIII brings out the fact that primary tuberculous pleurisy may start with high fever and shaking chill. Besides these types of tuberculous infection there are others even more confusing. It is possible for tuberculous pneumonia to start suddenly with a chill, high persistent fever, rusty sputum, and a high white cell count; and in all cases of pneumonia tuberculosis must be suspected when the temperature does not return to normal at the expected time. Of course, it is more common to have a story of previous lung involvement, an irregular fever, blood-streaked rather than rusty sputum, and only slight elevation of the white count. Other points to remember are that a tuberculous infection can be limited to the base of a lung, and miliary tuberculosis may present a very confusing picture.

**Case IX. Spontaneous Lung Abscess.**—Mr. M. S., aged forty, had no history of recent acute upper respiratory infection or sore throat, no recent operation on the tonsils, sinuses or teeth, and no known phlebitis or injury. Without previous symptoms he had a sudden chill, very severe left-sided pleural pain, and a temperature of 103° F. Pain persisted for ten days, but during this time there was little elevation of temperature and no cough. Two weeks after the onset he raised definite foul-smelling sputum with a few blood streaks. The temperature at this time was 101° to 103° F. The x-ray showed an abscess cavity 2.0 cm. in diameter in the left upper lobe with a moderate amount of lung involvement around it. Three weeks after the initial symptoms, two and a half cupfuls of foul sputum were raised in twenty-four hours. Sputum examination did not show pneumococci, Friedländer's bacilli, hemolytic streptococci, or spirochetes.

Six weeks after the onset the patient was admitted to a general hospital for surgery, but by this time his temperature was normal, he was raising less sputum, and the x-ray film showed some diminution in the size of the cavity. Improvement did not continue, however, and operation was performed.

This is a somewhat unusual case of spontaneous lung abscess without anything to account for its sudden appearance. It seems very unlikely that this was pneumococcus pneumonia from which an abscess developed. As in other similar cases in our series, the first symptom was acute pleural pain and the true diagnosis was not made until foul sputum appeared.

**Case X. Postoperative Atelectasis.**—Mr. A. D., aged forty-five years, was operated upon for hernia, and on the third postoperative day without a chill he developed a temperature of 102° F., moderate dyspnea, slight cyanosis, and discomfort but not true pleural pain in his left chest. He coughed and raised a moderate amount of homogeneous greenish sputum. This was examined and Type III pneumococci were found. The question was then raised as to whether we were dealing with a true postoperative pneumococcus pneumonia which should be treated by sulfapyridine. Physical examination showed dullness at the left base posteriorly with absent breath sounds. There was no definite evidence on physical examination of displacement of the mediastinum toward the affected side, but x-ray examination confirmed the clinical diagnosis of postoperative atelectasis by showing the triangular area of the collapsed left lower lobe and the heart and mediastinum displaced to that side.

The treatment indicated in this case was not sulfapyridine for Type III pneumococcus infection, but *postural drainage* to remove the "bronchial plug" and allow the lung to re-expand. The patient was placed on his right side with the foot of the bed elevated, and was encouraged to cough. Following this procedure he raised about a third of a cupful of thick sticky secretion, and examination of the left back, where there had been absent breath sounds before, now showed bronchial breathing—which is what one would expect to find over a collapsed lobe with the bronchus open. The next morning the temperature was normal, the bronchial breathing had disappeared and no further treatment was required.

True pneumococcus pneumonia may develop postopera-

tively, but in our experience nine-tenths of the pulmonary complications which occur in the first three or four postoperative days are *collapse* and not pneumonia or infarct. They should be treated by bronchial drainage rather than chemotherapy, even though Type III pneumococcus and some of the higher types are frequently found on sputum examination.

**Case XI.<sup>11</sup> Pulmonary Infarction.**—Mr. J. S., sixty-five years old, developed what he thought was “grippe.” He recovered quickly but, ten days later, he had a similar attack of malaise, followed in two days by sudden sharp pain in the right axilla involving the right shoulder and lumbar region. The pain was aggravated by cough and inspiration and he soon began to raise dark red blood mixed with mucus. There was no chill. When first taken the temperature was 100° F. and later rose to 100.5° F. The pulse ranged from 70 to 110. He was admitted to the hospital a week after the beginning of the second attack with a temperature of 98° F., pulse of 80, and respirations 20. The white cell count was 9,400, with 72 per cent polymorphonuclears. Sputum was bloody and not foul. There were signs of a moderate amount of fluid at the right base and on tapping this area bloody fluid was removed. After this the x-ray film showed a local area of density in the right costophrenic angle which, in the lateral film, proved to be in the posterior axillary line.

Because of the bloody pleural fluid some observers suspected malignancy, but *pulmonary infarct* with bloody fluid seemed a more likely diagnosis. Search was therefore made for a thrombophlebitis which could be the source of pulmonary embolus. Careful examination of the extremities, however, failed to reveal any evidence of peripheral phlebitis. On the third hospital day the patient complained of substernal pain and dyspnea. This was followed in ten minutes by cyanosis and air hunger. The cervical veins became dilated, the radial pulse could not be felt, the heart sounds became feeble and the patient died forty minutes later. Autopsy showed a massive pulmonary embolus, recent pulmonary infarction in

the right lower lobe, and organizing thrombophlebitis at the right popliteal vein.

Here is a case of sudden pleural pain, hemoptysis, and moderate elevation of temperature without previous operation or demonstrable phlebitis. Such cases are not infrequent and it is surprising how often the popliteal vein is the source of the embolus. If, as in some cases, the phlebitis can be localized after the occurrence of a small embolus and the vein tied off, a severe or fatal embolus may be prevented. In certain cases in the hospital series phlebitis with later pulmonary emboli have followed mild trauma to the extremities.

**Case XII. Incomplete Infarct.**—Mrs. R. D., aged twenty, had a partial miscarriage and was admitted to the hospital the following day for curettage. Two days later she had a slight cough and a temperature of 101° F. Three days after admission, the temperature rose to 103.2° F. and the pulse to 110. There was no pleural pain and no bloody sputum. On physical examination there were a few râles in the front of the chest on the right side. x-Ray films taken at this time showed an area of consolidation opposite the right lung root, roughly triangular in shape with a sharply defined margin and measuring 6.0 cm. in diameter. Two days later this area was much smaller and in four days, it had disappeared entirely and the temperature was normal.

On the basis of the clinical picture we regard this as an incomplete infarct which did not give pleural pain or bloody sputum. There is little doubt that such infarcts occur fairly frequently after various operative procedures and that they are often wrongly diagnosed as atypical pneumonia.

Pulmonary infarcts may appear after operation, with recognized phlebitis, trauma, cardiac conditions, or no obvious source, as in Case XI. True infarcts with necrosis of the alveolar walls and healing by organization seldom occur except with chronic pulmonary congestion; but incomplete ones, as in Case XII, with some air remaining in the alveoli, a less dense x-ray shadow, no necrosis of the alveolar walls, and early

resolution may occur without previous circulatory disturbance. Hampton and Castleman<sup>12</sup> report a recent series of pulmonary emboli checked by autopsy in which 40 per cent followed operation, 30 per cent were associated with cardiac conditions, and 30 per cent were in non-cardiac medical cases. Of the first group 50 per cent had pulmonary infarcts; of the second, 90 per cent; and of the third, 62 per cent.

In *typical infarct* there is pleural pain and friction rub, bloody mucoid sputum with few bacteria, moderate elevation of temperature (usually without chill), moderate elevation of white count, often orthopnea, and frequently cyanosis. However, infarcts, especially the incomplete ones, may have almost none of these features. Hampton and Castleman maintain that the x-ray shadow is not necessarily triangular, as has long been supposed, but that the infarct occurring at the periphery of the lung where two pleural surfaces meet assumes the shape of the part of the lung involved.

**Less Common Acute Pulmonary Conditions.**—Many less common acute pulmonary conditions have not been illustrated in this clinic. The following may be mentioned: (1) Pneumonia caused by other organisms than those noted, particularly *Friedländer's bacillus*; (2) the virus pneumonia of *psittacosis*; (3) pulmonary conditions associated with *rheumatic fever*, especially rheumatic pleuritis and arteritis, and possibly a hemorrhagic rheumatic pneumonitis; and (4) the pulmonary forms of *tularemia* and *undulant fever*.

One must keep in mind also that there is a danger of confusing certain chronic pulmonary conditions, particularly bronchiogenic carcinoma and bronchiectasis, with the acute ones already mentioned.

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### BLOOD DISORDERS: THEIR DIAGNOSIS AND TREAT- MENT IN GENERAL PRACTICE

WHEN *pallor*, *enlargement of lymph nodes* or *spleen*, or *hemorrhagic tendencies* are presenting symptoms of a blood dyscrasia, the clinician is fortunate in immediately receiving correct orientation. Such manifestations suggest a disorder of the blood and indicate further lines of study. When one reviews a series of cases of blood dyscrasias, however, it becomes apparent that the initial symptoms and signs all too often divert attention from, rather than direct it to, the blood. Minot, in a recent study<sup>1</sup> of 100 consecutive cases of pernicious anemia, found that the average time elapsing between the onset of symptoms and the establishment of correct diagnosis was over sixteen months, and in at least two thirds of the cases the presenting symptoms appeared referable to the cardiovascular, gastro-intestinal or central nervous system. *Fatigability*, *exhaustion*, *lack of a sense of well-being* and *weakness*, all common manifestations of anemia per se, are likewise to be found in many ailments. *Pallor* may not be manifest until late in the course of a blood disorder, and in women it is all too likely to be concealed at the common sites of inspection by lipstick, rouge and nail-polish. Examination of mucous membranes may be deceptive. Probably the most reliable guide to the hemoglobin concentration is to be found in an *inspection of the palmar surface* of the fingers and hands, provided the



inspection is made in a relatively warm room with the hands at or slightly below the level of the heart.

#### MINIMUM BLOOD STUDIES

Ideal though it might be, it is obviously impossible today for the average practitioner to make an extensive study of the blood. What, then, may be considered the *minimum* requirements in the way of blood examination in general practice if one is to make *early* diagnoses of blood disorders? Two simple procedures will suffice: an adequate *hemoglobin determination* and an inspection of a properly prepared and well-stained *blood film*. The Tallqvist method of hemoglobin estimation, although generally reliable in cases with well-marked anemia, often fails to detect an abnormal hemoglobin value in the very range in which it is most important, that is, in moderate anemia and in polycythemia. Any of the acid hematin methods, such as the Sahli, are convenient, simple, and sufficiently accurate for all clinical work.

**Preparation and Inspection of Blood Films.**—Blood films made by the apparently simpler slide method actually require more skill in order to obtain adequate preparations than do those made with clean cover slips. Although textbooks on hematology advocate elaborate methods of cleaning the glasses, tap water washing sometimes supplemented with a little soap, and an ordinary soft towel for drying, suffice to prepare the cover glasses unless they are exceptionally dirty. Although a differential count of the white blood cells is frequently necessary in order to make a diagnosis of the type of blood disorder present, a five-minute inspection of the stained films will generally be sufficient to exclude significant abnormalities.

The tendency to use the oil-immersion objective immediately is to be deplored. Its use may be compared to viewing an oil painting through a hand lens—one can see detail of texture and brush stroke, but not the picture. Under the low power objective, one may estimate the number of leukocytes. Significant leukopenia or leukocytosis is always apparent, although it is obviously impossible in many instances to tell

whether there are 5,000 or 10,000 white cells per cu. mm. Under the high power dry objective the red cells may be examined for abnormalities of size and shape; the number of platelets may be estimated with sufficient accuracy to know whether there is a significant thrombocytopenia or thrombocytosis; and a rough estimate may be made of the differential white blood cell count, and particularly whether abnormal white cells are present. When and if such cells are seen, then the oil-immersion objective may be brought into use. If the hemoglobin is within the normal range, and a study of the stained blood films as outlined above fails to reveal abnormalities, there is little likelihood that detailed hematologic study is indicated, or that such study will give important data for differential diagnosis.

**Other Diagnostic Measures.**—Having determined that an abnormality of the blood is present, the clinician will then obtain a red blood cell count, a white blood cell count, a differential white blood cell count and in many instances hematocrit and icteric index determinations, a reticulocyte count and a roughly quantitative urobilinogen estimation. Where indicated, x-ray examination will be made of the gastro-intestinal tract, chest, flat and long bones, and other regions. Gastric analysis and other special tests will be necessary in specific cases. However, it is to be emphasized that an adequate *detailed history* and a *complete physical examination* are of paramount importance in the differential diagnosis of blood disorders.

#### HYPOCHROMIC ANEMIA

**Blood Picture.**—This anemia, irrespective of underlying mechanism, is always characterized by a greater reduction in hemoglobin than in erythrocytes, so that there is a low *color index* (hemoglobin per cent  $\div$  red blood cells in millions  $\times 20$ ) which when below 0.7 is pathognomonic of hypochromic anemia. Stained blood films will reveal small, poorly stained erythrocytes with unstained large central areas. The *mean corpuscular volume* (hematocrit per cent  $\times 10 \div$  red blood cell count in millions) may vary from 50 to 70 cu. micra, in

contrast to the normal of 85 to 90 cu. micra. The *mean corpuscular hemoglobin concentration* (grams of hemoglobin per 100 cc.  $\times 100 \div$  hematocrit per cent) will lie between 21 and 29 per cent, in contrast to the normal of 33 to 35 per cent. No characteristic change occurs in the number of the white blood cells or platelets, although increases in each are not rare. The icteric index and urobilinogen excretion are generally normal or lower than normal.

In hypochromic anemia of long duration, soft, easily broken, flat or spoon-shaped fingernails are common. Atrophy of the papillae of the tongue is noted in some cases associated with gastric achlorhydria.

**Etiology and Incidence.**—With extremely rare exceptions, hypochromic anemias are due to a deficiency of available iron in the body. Although a deficient intake and poor absorption may both contribute to this deficiency, *blood loss* (either normal or pathologic) or *rapid growth* are usually required to produce a well-marked hypochromic anemia. Infancy and puberty with their attendant increases in body weight are frequently complicated by hypochromic anemia. Normal menses (approximately 50 cc. per period) in the course of five years will result in the loss of over 3 liters of blood; the effect of menorrhagia, hemorrhoids, and the like, is obvious. Each pregnancy depletes the mother not only of all the iron entering the fetus and placenta but of that in the blood lost at delivery.

Hypochromic anemia is the commonest type of anemia; it is encountered in 10 or more per cent of all women between the ages of puberty and the menopause.

When hypochromic anemia is encountered in the absence of an obvious cause, especially in men, *stool examinations for occult bleeding\** should be repeated frequently and a gastro-

\* A convenient maneuver at the time of the initial office examination consists in smearing the material from the gloved finger, following rectal examination, on a glass slide and performing a benzidine test on this material. A negative examination (check the benzidine solution with a drop of blood!) is generally significant. A positive reaction should be followed by routine testing with the patient on a meat-free diet.

intestinal x-ray examination should be made to exclude silent gastro-intestinal tract lesions such as diaphragmatic hernia and, particularly, benign or malignant tumors of the left half of the stomach or the right half of the colon; tumors at these sites frequently present severe hypochromic anemia as an outstanding manifestation long before they produce local signs or symptoms.

**Treatment.**—The treatment of hypochromic anemia consists in the oral administration of *iron* in adequate doses. Ferrous sulfate, 5 grains three times daily after meals, is so satisfactory that reference to other salts is hardly necessary, although Bland's pills U.S.P., in daily dosage of 60 grains, iron and ammonium citrates, 90 grains, or reduced iron, 45 grains, may be employed. Although many patients will respond satisfactorily to smaller doses of iron, the above-mentioned doses may be expected to produce a maximal response in all patients capable of responding to iron medication. Iron by injection is useless except in large (and frequently toxic) doses. Copper is of no importance in the *treatment of anemia in humans*, important as it is in animal experiments. Injections of liver extract are of no benefit in hypochromic anemia.

#### PERNICIOUS ANEMIA

**Gastro-intestinal and Neural Manifestations.**—The onset of pernicious anemia is almost always insidious. As noted above, symptomatology referable to the gastro-intestinal tract and central nervous system frequently precedes the development of obvious pallor. Every patient of middle age or beyond who complains of *indigestion*, *flatulence*, *anorexia*, "*gallbladder attacks*," *diarrhea* or *soreness of the tongue* must have the diagnosis of pernicious anemia excluded. Any patient with persistent *paresthesias* of the hands or feet together with severe anemia should be considered to have pernicious anemia until proved otherwise. The *numbness and tingling* of the extremities in this disorder differs from that encountered in many severe anemias, and in circulatory disturbances, in being relatively constant over long periods of time.

Other manifestations of the neural changes of pernicious anemia may suggest "neuritis," locomotor ataxia, fallen arches, or "rheumatism." Gross diminution of ability to perceive the vibrations of a tuning fork held in contact with the tibia is an almost constant finding in the neural lesion of pernicious anemia. *Reflex changes* vary from complete absence to extreme hyperactivity associated with clonus, depending on whether the lesion is predominantly in the posterior or lateral columns of the spinal cord. In the former, ataxia and a positive Romberg's sign occur; in the latter, spasticity and the sign of Babinski. Any combination of posterior and lateral column signs may be seen. However, pupillary abnormalities and changes in pain, light touch and thermal sensitivity probably never occur unless there is an associated polyneuritis. *Sphincter disturbances* are common in advanced cases. In the absence of well-marked blood abnormalities, lumbar puncture may be necessary to exclude syphilis of the central nervous system, spinal cord tumors, lesions of the cauda equina and prolapsed intervertebral disk.

**Blood Picture.**—The blood picture of pernicious anemia is characterized by a high *color index* (generally over 1.2), an increased *mean corpuscular volume* (110–160 cu. micra) and the presence of large oval macrocytes and occasionally tiny microcytes in the blood film, together with *leukopenia* and *thrombocytopenia*. The plasma pigments are usually increased with the *icteric index* 8 or higher and the indirect *van den Bergh reaction* positive, in contrast to hypochromic anemia where the icteric index is generally low and the van den Bergh reaction negative. The red blood cells may show practically any of the abnormalities known to occur except pronounced achromia. All forms of *abnormal shapes* may be present, the most bizarre being among the medium size and smaller cells. Diffuse and punctate *polychromatophilia* is common but reticulocyte counts above 5 per cent are unusual in untreated patients. With the decreased numbers of white cells the lymphocyte percentage is usually increased, and the polynuclear leukocytes generally are 4, 5 and 6 lobed.

Gastric anacidity occurs in 99 per cent of cases and an increased urinary urobilinogen excretion (in 1:16 dilution or higher) is observed in the majority of cases.

**Differential Diagnosis.**—Although the diagnosis is not difficult in the well-marked case of pernicious anemia, many other blood disorders, especially “aplastic” types of anemia, may simulate this condition.

An almost positive diagnostic check is afforded by the *therapeutic test*: From 30 to 75 or more units of liver extract are administered at a single intramuscular injection (this may be repeated daily for three to four days if desired, but often 30 units will suffice to initiate a remission). The reticulocytes are estimated on the first and subsequent days of treatment until a characteristic response has occurred or ten days have elapsed. Barring extremely rare cases with azotemia of severe degree or marked febrile sepsis, patients with true pernicious anemia with an erythrocyte level of 3.5 million per cu. mm. or lower will show a reticulocyte response. When the red cells are above this level, responses are so small as to be difficult to evaluate. The absence of a characteristic response at low levels is almost certain evidence that the patient does not have pernicious anemia. In practice, especially when the patient is being treated at home, it may not be feasible to obtain reticulocyte counts daily. In most instances, with the red cell count 2.5 million or below, reticulocyte counts made on the day treatment is started and on the fifth, sixth or seventh day thereafter will generally suffice to catch the elevation of the reticulocytes. *In determining whether a reticulocyte response is due to the liver extract given one must be sure that the patient is receiving no other form of therapy than liver extract.* Should one be administering iron, arsenic or other material simultaneously, it is impossible to tell what substance is responsible for the reticulocyte increase.

**Importance of Definite Proof of Diagnosis.**—Once the diagnosis of pernicious anemia is established, treatment must be life-long in order to supply the patient's deficiency in “liver extract” substance. If the disease is successfully treated, the

blood picture returns so completely to normal that diagnosis becomes impossible. Not infrequently, following acute concealed *blood loss*, a somewhat macrocytic type of anemia may be encountered. This anemia will in time disappear spontaneously, but mistaken for pernicious anemia it may be treated with liver. The blood, of course, returns to normal. Liver therapy then may be continued for years in the belief that it is needed. Should the patient seek evaluation of the problem it becomes necessary to omit liver therapy and observe whether signs of relapse develop. Since, in Addisonian pernicious anemia, these signs may not occur for a year or longer following omission of liver therapy, a prolonged period of observation may be required before a decision can be reached. Furthermore, should the patient have pernicious anemia, the onset of neural symptoms with severe irreversible changes may be the first indication. It, therefore, is of utmost importance that the diagnosis of pernicious anemia be definitely proved or disproved at the commencement of treatment.

**Treatment.**—The maintenance treatment of pernicious anemia consists in the administration of *liver*, *stomach* or *liver extract* at regular intervals and in adequate amount. A minimum of 1 U.S.P. unit per day should be given. Treatment by the *parenteral* route is usually most economical and convenient. It has recently been shown<sup>2</sup> that, although it is possible to inject at one time the amount of liver extract which when given in divided doses will maintain a patient in remission for a year, a considerable amount of this material is either destroyed or excreted, so that relapse occurs within a relatively short time. The physiologically ideal method of giving liver extract is by daily injection. This, however, is rarely practical and certainly not convenient. Patients generally desire to make the time interval between injections as long as possible. In our experience with several hundred cases we have found that four weeks is the maximum interval that should be permitted, and that, in general, injections at intervals of one to three weeks are preferable.

Ideally, the minimum amount to be injected should be the

equivalent of 1 unit a day. There is no doubt that less than this amount will suffice for many patients, particularly when the injections are given at one to two week intervals, but an amount larger than that which will merely maintain the patient's blood at a normal level makes for added safety. It is to be emphasized that not a few patients with pernicious anemia will require as much as the equivalent of 2 to 5 units daily as a maintenance dose. When complications of any sort develop, such as acute infections, or when neural manifestations are present, a *safe minimum* is 2 units a day, and the interval between injections should generally not exceed two weeks.

When liver extract in amounts adequate for the individual requirements of each patient with subacute combined degeneration of the spinal cord is employed, the results are most gratifying. Over a period of seven years, not a single relapse or unfavorable progression of signs or symptoms has occurred in a group of patients with this disorder so treated.<sup>3</sup> Indeed, striking improvement in many manifestations has been noted. Furthermore, it may be stated that neural lesions, so common in the improperly treated patient with pernicious anemia, never develop in the patient receiving adequate parenteral therapy.

#### HEMOLYTIC ANEMIAS

These may be *acute* or *chronic*.

**Acute Type.**—This is typified by the anemia which occurs in certain individuals following the ingestion of *sulfanilamide*. Within two to seven days after commencing the use of this drug, there occurs a rather precipitous drop in the number of red blood cells and the amount of hemoglobin, leukocytosis (which may go as high as 50,000 or more white cells per cu. mm.), frequently with immature forms, thrombocytosis, and an increase in the plasma pigments. Hemoglobinemia and hemoglobinuria occasionally usher in the attack in the more severe cases; the latter, producing a port-wine or darker colored urine, generally is the earliest sign that extensive acute blood destruction has occurred. In milder cases,



increased amounts of bile pigments are found in the urine, without actual free hemoglobin. Some cases of acute hemolytic anemia are ushered in by chills—this being particularly true of the idiopathic type not associated with drug or chemical ingestion.

*Treatment* consists in immediately stopping the administration of sulfanilamide or any other drug known to produce blood destruction, the forcing of fluids, the use of moderate amounts of alkalis to maintain an alkaline urine (in cases with frank hemoglobinuria in order to prevent the precipitation of hemoglobin in the tubular cells and lumina), and repeated transfusions of blood to restore and maintain the red blood cells at over 2,000,000 per cu. mm. Recovery is the rule with such therapy.

**Chronic Type.**—The atypical chronic hemolytic anemias will not be discussed. *Familial acholuric jaundice* (congenital hemolytic anemia) is the most common type of chronic anemia due to blood destruction. It is an inherited mendelian dominant character, present from birth but frequently not manifest by important symptoms until after puberty, and sometimes not until late in middle life. Hepatomegaly, splenomegaly, scleral and (in the more severe cases) skin jaundice, together with anemia, are found. There is an increased excretion of bile pigments in the feces, the urobilinogen content of the urine is very high, and the blood exhibits a normocytic normochromic anemia with many small darkly staining erythrocytes. The reticulocyte count is constantly elevated, as is the icteric index and indirect van den Bergh reaction, though usually fluctuating in degree. The characteristic diminished resistance of the erythrocytes to hypotonic saline is constant. Over 60 per cent of untreated cases develop bile pigment gallstones, frequently resulting in a complicating obstructive jaundice.

*Splenectomy*, although not affecting the increased fragility of the red blood cells, results in a rapid disappearance of jaundice and reticulocytosis and a return of the blood levels to normal, and greatly diminishes the likelihood of cholelith-

iasis. It is a procedure of little danger in this disorder and should be strongly recommended. These patients, frequently "more jaundiced than ill," are prone to temporize until complications occur and increase the hazard of operation. Patients as old as sixty years have been operated upon with complete success. Since manipulation of the spleen prior to its removal causes a considerable amount of its blood content to be returned to the circulation, it is frequently unnecessary to transfuse postoperatively. Neither iron nor liver extract is of value in this disease prior to splenectomy, although following operation a month's course of the former may be helpful.

### LEUKEMIA

The manifestations of leukemia are so protean<sup>4</sup> that brief discussion is all but useless. Symptoms and signs will depend on the localization of the lesions.

**Acute Leukemia.**—Acute leukemias rarely present striking enlargement of the lymph nodes or spleen. Fever of unexplained origin is common. Ulcerative lesions of the mouth and gums are frequent, especially in the monocytic type. Anemia, generally slightly macrocytic, and thrombocytopenia are the rule. In most instances, whether there be an increase in the number of white blood cells or not, there will be numerous very immature forms present, easily recognizable by the rather scanty dark blue cytoplasm and the nucleoli in the large deeply staining nuclei.

*Differentiation* of acute leukemia from *infectious mononucleosis* is of considerable importance and may present many difficulties. In the latter the enlarged nodes are frequently tender to palpation, in leukemia less commonly so. Anemia and thrombocytopenia are not found in this benign disorder, although ulcerating lesions of the mouth and throat occur. The sheep-cell agglutination test becomes positive after a matter of a few days to a week in infectious mononucleosis and then serves to differentiate the two disorders.

In acute leukemia, repeated transfusions of blood may be

of temporary value. Irradiation is contraindicated. In infectious mononucleosis, symptomatic treatment is all that is required.

**Chronic Myelogenous Leukemia.**—This type of leukemia generally manifests itself by splenomegaly and an increase in the number of white blood cells, with polymorphonuclears and all stages of myelocytes predominating. Anemia may be absent or mild early in the disease.

Leukemia is to be *differentiated* from *leukemoid reactions with hyperleukocytosis*, which may simulate the blood picture of leukemia closely. In these conditions splenomegaly is rare, myelocytes, though present, are usually not as numerous as in leukemia, and the history and general examination will frequently reveal the etiology of the hyperleukocytosis in such conditions as sepsis, hemorrhage plus infection, and carcinoma, particularly with widespread metastases in many organs including the liver.

*Treatment* in leukemia should be directed at the patient, not the white blood cell count. Patients may be relatively asymptomatic, with white cell levels of 50,000 per cu. mm. or more. When *x-ray therapy* can be employed this is the treatment of choice, an endeavor being made to reduce the size of the spleen, diminish the white blood cell count, and restore the red cell count and hemoglobin value to a normal level. If *x-ray treatment* is not available or if it fails to influence the manifestations of the disorder, *Fowler's solution* should be administered with caution, commencing with 3 minims three times daily and increasing by 1 minim daily, until the first signs of intoxication appear. When these signs, such as nausea, swelling of the eyelids or chemosis, burning of the hands or feet or skin rashes are observed, the drug should be omitted for four to six days and then resumed in small daily doses. Rarely should more than 15 minims three times daily be given.

**Chronic Lymphatic Leukemia.**—This form usually manifests itself by lymphadenopathy, anemia and an elevated white blood cell count, with 90 or more percent of cells being small lymphocytes. Enlargement of the spleen and liver,

although frequently present, is not often as marked as in myelogenous leukemia.

*Treatment* of chronic lymphatic leukemia should be by irradiation. If there is severe anemia, transfusions of blood should be employed to bring the hemoglobin level above 50 per cent before x-ray treatment is commenced. Not uncommonly chronic lymphatic leukemia, without anemia or lymphadenopathy of note but with leukocyte counts as high as 60,000 per cu. mm., is an incidental finding in elderly individuals who consult a physician for definitely nonleukemic symptoms. Treatment is not indicated in such cases until such a time as anemia or lymph node enlargement appears or lymphomatous infiltration of organs interferes with vital functions. Often such elderly individuals succumb to other ailments before serious leukemic manifestations appear.

#### HEMORRHAGIC DISORDERS

These conditions may be divided into three main groups: *vascular purpuras*, *thrombocytopenic purpuras*, and *disorders of blood coagulation*.

**Vascular Purpuras.**—In this group are to be found the arteriosclerotic type, the so-called "allergic" type (*Schönlein-Henoch's purpura*), the type associated with acute infections, and that due to a lack of vitamin C. *Vitamin C deficiency (scurvy)* is characterized by the appearance of minute purpuric spots about the hair follicles, especially in the legs, and by the presence of swollen, purplish, easily bleeding gums. Normocytic, normochromic anemia, entirely out of proportion to the amount of bleeding, is common. Vitamin C content of the blood is low or entirely absent. The *capillary fragility test*, performed by placing a blood pressure cuff on the upper arm, inflating to midway between systolic and diastolic pressures and maintaining at this level for ten minutes, is positive as evidenced by the appearance of more than 10 petechiae per sq. cm. in the skin of the forearm 3 to 5 cm. below the elbow crease. This test, however, is also positive in thrombocytopenic and certain other purpuras. *Treatment of scurvy* con-

sists in the daily administration of large quantities of orange juice (8 to 16 ounces) or of from 150 to 1,000 mg. of ascorbic acid, either orally or by injection.

**Thrombocytopenic Purpura.**—This condition may be a manifestation of leukemia, aplastic anemia or myelophthisis of various types, a reaction to certain drugs such as sedormid, or it may occur as a disorder of unknown etiology referred to as *idiopathic thrombocytopenic purpura (Werlhof's disease)*. All types of thrombocytopenic purpura are characterized by diminution in the number of platelets, increased capillary fragility, prolonged bleeding time, normal clotting time, and poor or no clot retractibility.

**Treatment.**—In every case the exclusion of primary causative disorders is of first importance, followed by a careful history of drug ingestion, particularly of *sedormid*. In the secondary types, transfusion may be necessary, in addition to the treatment of the primary disorder. Purpura from the ingestion of sedormid will disappear following discontinuance of the use of this drug, although transfusion may be necessary to support life until recovery of normal numbers of platelets occurs. Idiopathic thrombocytopenic purpura may be acute, recurrent or chronic. The acute cases require only transfusion as often as necessary. Under such treatment the majority recover, although certain patients run a progressive course to death in spite of all measures taken. The chronic and recurrent forms are most often benefited by *splenectomy*, although the hope of complete cure should not be held out in these cases. Snake venom, x-ray treatment, ascorbic acid and parathormone, among many suggested forms of treatment, have given disappointing results.

**Hemophilia.**—Hemophilia is a sex-linked, recessive inherited disease occurring only in males born of "carrier" mothers. Capillary fragility, bleeding time and platelet counts are normal but the *coagulation time of the blood is always prolonged*, often to an hour or more. Clot retractibility and "prothrombin time" are normal. *Hemorrhages into joints*,

frequently associated with a febrile course, are sometimes mistaken for a variety of other conditions.

*Treatment.*—Although the management of cases of hemophilia rarely devolves upon the general practitioner, it is worth pointing out that hemophilic individuals do travel in automobiles and seem unusually prone to become involved in accidents in areas remote from physicians well acquainted with the condition. Under these circumstances, in addition to all local measures to control bleeding, the intravenous administration of from 50 to 100 cc. of *compatible human blood* can be relied upon to reduce the clotting time,<sup>5</sup> temporarily at least. This procedure may be repeated as often as is necessary. Should the loss of blood be considerable, a 500 to 800 cc. *transfusion* should be given. This amount of blood will ordinarily reduce the clotting time for sixteen hours or longer. It may well be pointed out that there is no danger in venipuncture or intravenous medication in hemophilia if the usual precautions are taken. The local application of *active* thromboplastic substances is valuable if the material can be supplied in relatively concentrated form to the actual bleeding area. Parenteral or oral administration is of little or no value.

**Other Disorders of Blood Coagulation.**—Prothrombin deficiency is a feature of many cases of *hemorrhagic disease of the newborn*.<sup>6</sup> Although the prothrombin concentration of infants' blood at birth is 60 to 75 per cent of the adult level, it often drops abruptly during the first few days of life. Recovery of normal levels is usually prompt and occurs spontaneously, except in certain infants who exhibit external or internal bleeding and have an exceedingly low prothrombin concentration in the blood as determined by the method of Quick.<sup>7</sup> Although recovery may occur spontaneously, it can be hastened by the oral administration of vitamin K.

In adults, prothrombin deficiency characteristically occurs from malabsorption of vitamin K as a result of *obstructive jaundice*, bile salts being essential for the absorption of this vitamin from the gastro-intestinal tract. It may also occur in severe *liver disease* apart from biliary obstruction, from

*dietary deficiency*, and from malabsorption in ulcerative and other forms of *colitis*, *idiopathic steatorrhea*, *celiac disease* and *sprue*. When the prothrombin deficiency is marked, bleeding and coagulation times are moderately prolonged. Capillary fragility, platelet counts and clot retractibility are normal.

*Treatment.*—In cases of obstructive jaundice with prothrombin deficiency, it is necessary to administer bile salts as well as vitamin K to restore prothrombin values to normal. The synthetic material (2-methyl-1,4-naphthoquinone), in daily doses of 1 mg. with 1 to 2 gm. of bile salts, will markedly elevate the prothrombin concentration within twenty-four hours, provided severe liver damage is not present. A new synthetic water-soluble derivative of this substance will produce an increased prothrombin concentration within a few hours after intravenous administration.

#### BANTI'S DISEASE

The combination of anemia, leukopenia and splenomegaly, when not due to some well-recognized condition, has been described as Banti's disease. It has been shown that the splenomegaly of these patients is due to splenic vein hypertension, either from thrombophlebitis of the splenic or portal veins or cirrhosis of the liver. The anemia is either hypochromic as a result of hemorrhage from varices, in which case it will respond to iron therapy, or normocytic from liver cirrhosis, in which case it will respond to no known therapy. Splenectomy will not prevent the development of hepatic cirrhosis in these patients, as they already do or do not have it; if they do not, there is no more likelihood of their getting cirrhosis than individuals without enlarged spleens. The value of splenectomy in preventing recurrent hemorrhages from gastric or esophageal varices is doubtful.

#### CONCLUDING REMARKS

The foregoing remarks are intended simply to serve as guiding notes to the general practitioner of medicine concern-

ing some aspects of the commoner disorders of the blood. No reference has been made to polycythemia, lymphomata other than lymphatic leukemia, aplastic and related types of anemia, agranulocytosis and many other disorders of the blood, which are of relatively less frequent occurrence.

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## CLINIC OF DR. GEORGE C. PRATHER

BOSTON

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### RECURRENT PYELONEPHRITIS

INFECTION is probably the most common malady of the urinary organs. It is not surprising, therefore, that clinical considerations of this problem are discussed repeatedly. We, as practicing physicians, encounter not only the acute phase of urinary tract infection, but also the so-called chronic or recurrent types, which I believe is the subject for comment at this time.

#### CASE HISTORY

Discussion today concerns a married woman, thirty-one years of age, whose *primary symptoms* are pain in the right side of the abdomen and recurrent fever. Her *past history* discloses no pertinent information indicative of renal disease during childhood. The exanthemata were not followed by prolonged convalescence or complications. She did not have recurrent fever or frequent illness as a child, and she cannot remember having had pain in the regions of the costovertebral angles. The appendix was removed when she was nineteen years old. Catamenia began at a normal age, and has been regular and without abnormal discomfort since onset.

She was married at the age of twenty-four. Two years later, during the sixth month of her first pregnancy, she developed a fever associated with pain in the right flank and pyuria. Her physician said she had pyelitis, advised bed rest and plenty of liquids, and prescribed some white tablets as medicine. Her fever lasted five days, and she had no recurrence of symptoms during the remainder of the pregnancy. Delivery of a seven-pound baby was accomplished with the

aid of low forceps. The puerperium was uncomplicated except for a mild febrile reaction for three days after delivery. Postpartum check-up by her physician six weeks later included inquiry regarding flank pain, fever, and bladder irritability, but a catheter specimen was not taken for examination.

**Illness During First Pregnancy.**—Commenting for a moment on her illness during her first pregnancy, we shall certainly agree with the diagnosis which her physician made at the time—*pyelitis*—except for the fact that present-day terminology practically excludes the word “pyelitis,” using instead the term *pyelonephritis*. Modern urological texts speak only of “pyelonephritis”; for example, Keyes, in his recent book, holds that since the clinician does not see pyelitis without bacterial nephritis, “the term pyelitis is a misnomer.” There is therefore now general agreement in the urological field that the term “pyelonephritis” offers a better description of the renal condition than does “pyelitis.” The fact that kidney substance, as well as the kidney pelvis, is involved in the inflammatory process, and in addition, the fact that the renal parenchyma is permanently involved in many cases of pyelonephritis, demonstrates that if we are accurately to describe both the pathologic and clinical picture, we should use the term “pyelonephritis” instead of “pyelitis.”

If we may agree upon this term, then, other general considerations bearing upon this case should next be mentioned: Pyelonephritis during pregnancy has an incidence of 1 to 2 per cent if calculated from the data of a fairly large maternity hospital. We know that primiparas develop renal infection more frequently than multiparas. Perhaps this is true because the tense abdominal wall of the primipara induces more uterine pressure on the pelvic portion of the ureters, thereby causing stasis of urine in the renal pelves and upper ureters. It is well known that the right renal pelvis and upper ureter show moderate to considerable dilatation during the latter half of pregnancy in practically all normal women, while the left upper ureter and renal pelvis show a similar change in 50 to 60 per cent.

*Hormonal and Mechanical Causes of Urinary Stasis.*—At least some of the dilatation or atony of the upper urinary tract in pregnancy is explained on a *hormonal* basis, because of the fact that a change in this direction is demonstrable before the enlarged uterus becomes a mechanical factor. Traut and his associates, working with the Trattner hydrophorograph, recorded the frequency and amplitude of contractions of the ureter and renal pelvis during pregnancy. They were able to demonstrate diminished peristaltic activity of the ureter and renal pelvis very early in pregnancy before the uterus was large enough to exert a mechanical influence on the ureters. Additional evidence in favor of hormonal influence was presented by one Italian worker who made a concentrate of the blood of pregnant rabbits, took intravenous pyelograms of nonpregnant rabbits before and after injecting the concentrate, and found that ureteral dilatation occurred for a short time following the injection of the concentrate of blood from pregnant animals. Unpublished work from New Haven, Connecticut, by Jenkins, indicates that ureteral dilatation seen by intravenous pyelography in pregnant monkeys can be maintained through the remainder of the pregnancy even though the fetus is removed by hysterotomy, provided the placenta is left intact in utero. These interesting observations indicate the presence of a blood-borne substance which occurs during pregnancy and produces relaxation or atony of the upper ureter and renal pelvis. The exact nature or source of this hormone has not been determined.

Evidence obtained by pyelography, as well as by autopsy, proves that in the last four months of pregnancy the ureteral dilatation stops abruptly at the brim of the bony pelvis where uterine pressure on the ureter is greatest. It is difficult to explain how an endocrine substance can produce the unequal degrees of dilatation between the right and left ureters seen so frequently in pregnant women, or why the lower third of the ureters do not take part in the atonic endocrine influence. Therefore, the *mechanical* as well as the endocrine theory must be recognized.

It is not surprising that with urinary stasis in the renal pelves, pyelonephritis develops. Stasis anywhere in the urinary tract is conducive to urinary infection. Mechanical obstruction, of course, is the most frequent cause of stasis in the urinary tract. The obstruction can be congenital, as seen in congenital valves of the posterior urethra in the male infant or child, as found in congenital strictures of the lower ends of the ureters, or as demonstrated by aberrant vessels at the ureteropelvic junction. The obstruction is very frequently acquired by renal or ureteral stones or, for example, by prostatic obstruction. The stasis found in the upper urinary tract during pregnancies and tends to resolve after delivery. Various mechanical conditions which exert an influence on urinary tract infection either by creating a situation favorable for infection or by exerting an adverse influence toward an immediate cure are spoken of as "accessory factors." It is evident that accessory factors play an important part, not only in the occurrence of pyelonephritis, but also in the failure of complete and permanent recovery from it. As we have indicated, they can be congenital, acquired, or physiologic in origin.

**Infected Urine Following First Pregnancy.**—The patient under discussion was fortunate in making a good recovery from her pyelonephritis of pregnancy under sound, conservative medical treatment, but it is probable that her urine remained infected during the remainder of the pregnancy even though she had no fever, pain, or bladder discomfort. We have found that while the patient's symptoms disappear following acute febrile pyelonephritis, the urine is likely to remain infected until after delivery unless careful treatment with *mandelic acid* or *sulfanilamide* is instituted. Even with these agents, it is not always possible to sterilize the urinary tract of every patient during her pregnancy. Pregnancy offers a severe test for any drug designated as a urinary antiseptic.

While many patients who have had pyelonephritis during pregnancy will clear their urines bacteriologically during a four-month period after delivery, it is not wise to take this clearing for granted *simply because there are no symptoms.*

A catheter specimen examined for bacteria as well as leukocytes is the only reliable method of determining the presence or absence of a pyelitic type of infection. We do not know, therefore, whether the pyelitis was cured following the first pregnancy of our present patient. According to her history, she remained well until the seventh month of her second pregnancy two years later, when she again developed "pyelitis." Since this attack did not subside within a week, she was hospitalized. Cystoscopic and pyelographic study (Fig. 166) in-

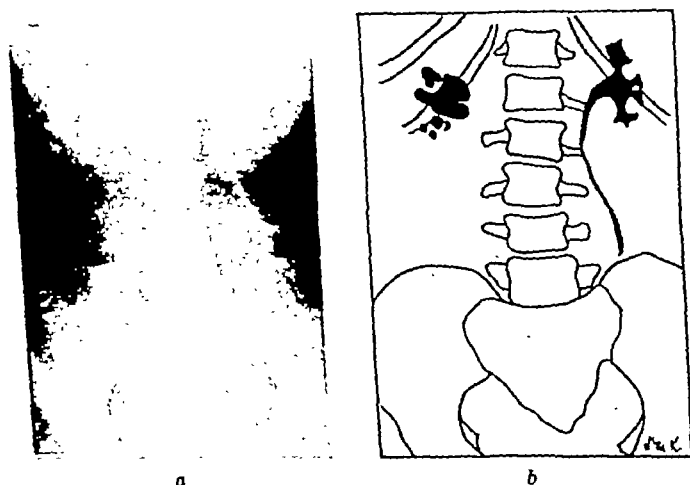


Fig. 166.—*a*, Intravenous pyelogram during seventh month of second pregnancy, showing dilatation of right renal pelvis. *b*, Diagram of pyelogram.

licated dilated kidneys and ureters with infection in the right kidney. Lavage of the renal pelvis, forced fluids, and alkalis brought about improvement, so that the patient continued to term without further trouble. These events occurred before mandelic acid and sulfanilamide were available as urinary antiseptics. Patients usually recovered from their fever, and many recovered completely after delivery without these two drugs. Absence of congenital or acquired accessory factors, such as stone, ptosis, aberrant vessels, plus individual immunity, will allow many urinary tract infections to clear spon-

taneously. Today, mandelic acid or sulfanilamide therapy will at times produce a urine bacteriologically negative during the administration of the medicine even where there is some urinary stasis due to accessory factors as mentioned above. The apparent cure is, however, only temporary, if urinary stasis is present. In order to be sure of our permanent results, we must examine a urine specimen *several weeks after medication has been stopped*. Perhaps we shall have a chance later in this discussion to make further comments about the choice of urinary antiseptics.

#### Course from Second Delivery to Present Illness.—

Our patient felt well after her second delivery, and did not return to her physician for a check-up as advised. During the next three years she occasionally noticed a dull aching pain in the right costovertebral region or the right mid-abdomen. This symptom occurred particularly when she was nervously tired, and it was frequently accompanied by lack of appetite. She had not taken her temperature, but stated she had had no chills until just before the present admission to hospital. A few days ago, the pain previously described returned. She felt chilly and nauseated, and she vomited once. Her temperature at home was found to be 100.6° F. Her physician found no physical signs except tenderness to palpation and questionable spasm in the right mid-abdomen and flank. Hospitalization was suggested and accepted.

#### DIAGNOSIS

**Findings on General Examination.**—From the history beginning with pyelonephritis during pregnancy, to and including the present illness, it is likely that a chronic pyelonephritis with flare-ups explains the clinical picture. We must examine the present physical signs, laboratory findings, and other data in order to come to a definite conclusion concerning diagnosis and suggestions for treatment. *Physical examination* indicates teeth in sound condition, although we cannot rule out apical abscesses without dental x-rays—foci of infection as a cause of recurrent pyelitis cannot always be demonstrated but are

worth remembering in an obscure problem. Sinuses are said to transilluminate normally. Examination of heart and lungs is reported as normal. Blood pressure has been determined as 128-136 systolic, with 78-82 as the diastolic readings. In spite of the normal blood pressure findings in this patient, it may be worth while to digress for a few moments to discuss recent data regarding hypertension.

**Hypertension.**—Hypertension today is regarded as a symptom rather than a disease. In many instances we may know the pathologic changes which are manifested by the patient, but we are ignorant of the cause. However, renewed interest in the possible relation of unilateral, as well as bilateral, renal disease to hypertension can be credited to brilliant work in the experimental field as well as in the clinical reports which have followed. *Ischemia* of the kidney plus perhaps some *pressor substance* produced by the ischemic kidney is now recognized as a situation which can produce hypertension.

The reason for bringing this point up for comment even though the patient under discussion has no hypertension is the current interest in the relation between long standing pyelonephritis and hypertension. Weiss and Parker in a recent monograph have presented evidence to the effect that pyelonephritis, if not cured, may progress to the atrophic type of pyelonephritis with a contracted kidney and hypertension. Unilateral disease of this type with hypertension has been described, and patients have been relieved of their hypertension by nephrectomy of the atrophic kidney. As the result of the brilliant experimental work relative to a renal type of hypertension, and the possible cure by nephrectomy in certain selected cases, the present trend is toward studying patients with hypertension very carefully to see if a unilateral renal factor can be demonstrated. Furthermore, the recent data relative to hypertension and pyelonephritis make it imperative not only to have a detailed diagnosis in patients with renal infection, but also to treat and follow them to a cure. The day when urotropin or some similar drug was given for pyelitis



or cystitis without consideration of the type of bacteria, the quantity of fluid, the urinary pH, or follow-up examination of suitable specimens seems obsolete at present if one is conscientious in protecting the future health of the patient as far as possible. While it is not always easy to obtain cooperation from the patient with urinary infection who is symptom-free, the seriousness of the situation does not have to be exaggerated to be impressive. The few remarks for which we have time regarding the present ideas about kidney disease and hypertension fail to do justice to the scientific and clinical progress of the present and immediate past. Much more will, no doubt, be contributed in the future. We must not conclude, however, that every patient with hypertension will have a type of renal disease which can be cured by surgery. In fact, opinion at present indicates that only about 5 per cent or less will fall into the group in which the hypertension is due to unilateral renal disease. In order to discover the small group of patients who might benefit by renal surgery, it will be necessary to have complete roentgen and functional studies of the kidneys and lower urinary tract in all patients with consistently high blood pressure. So much digression, however, though justified because hypertension is so important a side issue of pyelonephritis, has probably caused us to forget that we were discussing the physical examination of our patient.

**Abdominal Findings.**—Returning now to the abdominal findings in our patient, we can say that palpation disclosed no evidence of distention and no mass. Tenderness in the right mid-abdomen, higher than McBurney's point, is slight but definite. The right upper quadrant is also tender when it is palpated concomitantly with one hand at the right costovertebral angle. There is slight tenderness in the right costovertebral angle. No tenderness can be demonstrated in the lower abdomen. The appendix scar is well healed. *Pelvic examination* finds a moderate cystocele, but no evidence of ovarian cyst, enlarged uterus, or inflammatory disease which might cause continued obstruction in the pelvic ureter. A cystocele which permits a bladder residual (after voiding) of more than 1

ounce can be an important factor in persistent urinary infection. It is feasible to catheterize the patient immediately after voiding, as one does in examining a man with prostatism, to determine an appreciable residual.

**Urinary Findings.**—A *catheter* specimen of urine; which is the only reliable sample from a female, is reported as showing the slightest possible trace of albumin, no sugar, specific gravity of 1.012, pH 6, and a centrifuged sediment containing numerous motile bacilli, 25 to 30 white blood cells, and a rare red blood cell in each high power field. The stained sediment shows the bacilli gram-negative. The slight amount of albumin can be explained by the high content of bacterial bodies in the urine, although infected urines often show no albumin by qualitative test. The specific gravity of 1.012 can be accounted for by a liberal intake of fluids, although this cannot be proved without doing some form of concentration test. The pH 6, slightly acid, is consistent with the *B. coli* type of infection demonstrated by culture. The sediment speaks for itself, indicating urinary infection, but not disclosing its source.

**Blood Counts and Other Data.**—Blood counts show a leukocytosis of 12,000 but are otherwise normal. The non-protein nitrogen is reported as 34 mg. per 100 cc. of blood, and the blood sugar is reported as 110 mg. per 100 cc. Blood Wassermann is negative. The two-hour *phenolsulfonphthalein* test, after intramuscular injection, finds an excretion of 65 per cent, which is normal. The *urea clearance* test is reported as 80 per cent of normal, while our concentration test indicates a specific gravity of 1.022 in one specimen.

**Renal Function.**—Though this patient has normal values for the various tests of total renal function, the subject of renal function deserves comment. Our information of renal function is closely linked with the available data on renal physiology. You will recall that each kidney is composed of many nephrons (glomerulus with its contiguous tubule). Moritz and Hayman have estimated that there are about 1,283,000 nephrons in each kidney. Our present conception of renal

physiology indicates that filtration of protein-free liquid takes place in the glomerulus, the glomerular membrane acting as the filter. This process of simple filtration from the capillaries in the glomerulus into the capillary space is dependent to a major extent upon the impulse of each heart beat. The filtrate then continues through the tubular channel of its own nephron until in larger collecting tubules it merges with urine which has come from other nephrons, emptying ultimately into the renal pelvis. During the progress of the filtrate through the various sections of the tubules; you will recall that, according to Cushny's theory of urine formation, tubular reabsorption of certain elements takes place. Richards and his co-workers have, by ingenious methods, been able to demonstrate in animals the concept of both glomerular filtration and tubular reabsorption. Cushny did not believe that tubular secretion took place. Most students of renal physiology today are convinced that active secretion by the cells of certain parts of the tubules occurs, contributing material into the lumen of the tubule. Marshall has done brilliant work in demonstrating this phase of tubular activity. We may conclude, therefore, that urine formation by the kidney takes place by way of *glomerular filtration*, *tubular reabsorption*, and *tubular secretion*.

It is obvious that renal function can be influenced by conditions which affect certain or all of the nephrons as units, by conditions which affect only parts of each nephron (glomerulus or tubule) or by conditions affecting the circulatory impulse to part or all the nephrons.

**Renal Function Tests.**—It will be impossible at this time to discuss the pathologic physiology of the kidney, but we should review the more common renal function tests used today in clinical medicine. We shall take up briefly:

1. Concentration specific gravity test
2. The urea clearance test
3. The phenolsulfonphthalein test.
4. Blood chemistry tests

**Specific Gravity or Concentration Test.**—The specific gravity or concentration test is easy to perform, and along with

the urea clearance determination, offers as delicate a test for slight disturbances of renal function as we have in clinical practice. The concentration test gives an estimate of tubular function. If liquids are restricted for a period of eighteen hours, normal kidneys will be able to produce urine with a specific gravity of 1.020 to 1.032 toward the end of the eighteen-hour period. A fixed or constant specific gravity of 1.008 to 1.012 in all urine specimens during the period of the test would indicate severe renal damage.

*Urea Clearance Test.*—The urea clearance test, developed by Van Slyke and co-workers several years ago, is acknowledged as a delicate test for renal function but requires the assistance of a capable laboratory technician. Because of the fact that the rate of excretion of urea in the urine is partially dependent on urinary volume, it is customary to quote the result in terms of per cent. Values of 75 per cent or above are considered to represent normal renal function, while those between 60 to 75 per cent are in a doubtfully normal state. It is said that when the urea clearance is less than 20 per cent of normal, the blood urea nitrogen of the blood is nearly always elevated.

*Phenolsulfonphthalein Test.*—The phenolsulfonphthalein test, while not the most sensitive of our renal tests, is simple to perform and has been used extensively in urology since Geraghty and Rowntree presented their idea about twenty-eight years ago. A simple standard colorimeter is used. One ampoule of the dye (6 mg.) is injected intramuscularly or intravenously after the patient voids. The patient drinks two glassfuls of water immediately. Urine is voided or collected one hour and ten minutes after intramuscular injection and is labeled "first hour specimen." Two hours and ten minutes after the injection of the dye, the second specimen is voided or collected. Each specimen is made alkaline, diluted to 1000 cc., and compared with the colorimetric standards. Normal excretion after intramuscular injection is 40 to 60 per cent during the first hour; 20 to 25 per cent the second hour. Following intravenous injection of phenolsulfonphthalein, 40 per

cent should be excreted during the first half-hour. Delayed excretion may indicate diminished renal function.

*Blood Chemistry Tests.*—Nitrogenous substances in the blood, such as urea nitrogen or nonprotein nitrogen, serve to indicate whether renal excretion is sufficient to keep even with or ahead of nitrogen metabolism of the body. These tests are only very rough tests of renal function, yet the standards which they represent are important in present-day medicine. When these values are elevated, we may say renal function is *decom-*

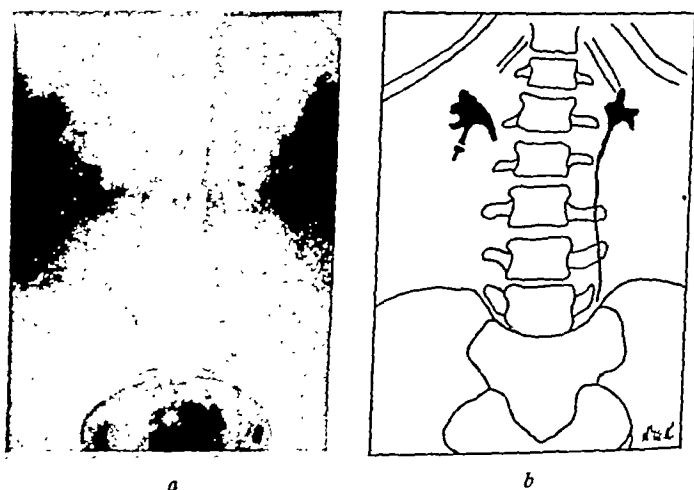


Fig. 167.—*a*, Intravenous pyelogram on hospital admission, showing indication of pathology in right kidney, especially at upper pole. *b*, Diagram of pyelogram.

*pensated*—the danger signal has been raised. As with the phenolsulfonphthalein test, prerenal deviation of fluids, as well as changes in the cardiovascular system, influence these tests adversely even though renal function is relatively good. The normal nonprotein nitrogen level in the blood is normally 30 to 40 mg. per 100 cc. Blood urea nitrogen is usually about one-half of the nonprotein nitrogen.

The patient under discussion has a total renal function which is normal. In order to reach a diagnosis to find the

cause of long standing or recurrent pyuria, and the right flank discomfort, we need the help of *x-ray data*:

**x-Ray Findings.**—Under the circumstances, we might go directly to cystoscopic study or find what information can be obtained from *intravenous pyelography*. The latter method was used here, fluids being restricted during the fifteen hours preceding the examination in order to obtain the best concentration of the dye in the kidney. The films indicate retarded secretion by the right kidney; prompt secretion by the left kidney (Fig. 167). Delayed secretion following injection of the intravenous dye for intravenous pyelography indicates impaired renal function at the particular moment, although in cases of obstructive uropathy it does not give accurate evidence of the integrity of the kidney following relief of the obstruction. Frequently, when both kidneys are normal, the best concentration of the dye in the kidney is seen during a five- to fifteen-minute period following injection.

The *left* kidney appears to be normal; the *right* shows some blunting of the calyces; the suspicion of an abnormal upper pole and calyx. The examination, therefore, reveals a normal left kidney and points to anatomic pathology with diminished function of the right kidney. Before deciding whether medical or surgical treatment is indicated, however, we need the help of cystoscopic study:

**Cystoscopic Examination.**—This should tell us if the urinary infection is limited to the right kidney and bladder, or whether both kidneys are a source of infection with pain only from the right. Differential functions of the kidney can be checked with ureteral catheters in place, and retrograde pyelograms can be obtained. Data from cystoscopy demonstrate that the urine from the right kidney contains leukocytes and bacteria which on culture show a profuse growth of *B. coli*. The left kidney urine contains only a rare leukocyte, and the culture is reported as showing no growth. The left kidney has an excellent response to function tests, while the right kidney appears nearly functionless in comparison. The retrograde pyelograms are of great interest. The anatomic condition of

the right kidney is shown in much better contrast than in those obtained by secretory pyelogram (Fig. 168). In addition, the retrograde films demonstrate a dilated upper calyx with only



Fig. 168.—Retrograde pyelogram on hospital admission, indicating extensive pyonephrosis, especially upper pole of right kidney, with inflammatory changes in upper ureter.

a thin rim of cortical tissue at the upper pole of the right kidney. Lack of function in the upper part of the kidney explains the failure of the secretory films to demonstrate this pathology.

#### TREATMENT

Of course, stasis of urine in this part of the kidney, in addition to the probable pyelonephritic changes in the other portions of the kidney, definitely places this patient in a group difficult to cure by medical measures. *Surgery* in this instance should offer an excellent chance of cure, not only of the pyuria, but also of the pain referred to the right flank.

**Urinary Antiseptics.**—If our diagnostic studies had not

revealed the gross anatomic changes in the right kidney with diminished function, we should naturally endeavor to clear up the urinary infection with suitable medication. At present, our two most potent drugs acting as urinary antiseptics for *B. coli* infection are *mandelic acid* and *sulfanilamide*. It is difficult to say which is the more effective. Both have their good points and their weak points. We can mention a few personal conclusions which may act as a guide: Mandelic acid with the necessary restriction of fluids for efficacy is not so useful in acute febrile urinary infection when a liquid intake of 3000 cc. a day or more is desirable. We have found sulfanilamide effective, at times, in daily doses of 60 grains with a liquid intake of 3000 cc. daily. At times sulfanilamide appears to be effective even though the blood and urine levels of the drug obtained by this dosage are low.

The afebrile chronic or subacute *B. coli* urinary infection is suitable for either mandelic acid or sulfanilamide medication, provided the accessory or anatomical factors have been excluded. The various possible side reactions or complications occasionally experienced with sulfanilamide may make mandelic acid therapy safer unless the patient can be observed frequently. When one of these drugs fails in a certain patient, the other may be effective. Both of these drugs are more effective than the preparations used previously, which were rarely powerful enough to produce a clear urine when anatomical obstruction or stasis was present in the urinary tract. It is not unusual to find either sulfanilamide or mandelic acid therapy successful in producing a clear urine during the period of medication only to have examination of a urine specimen several weeks later disclose a recurrence of the infection. One should, therefore, always examine the urine a month after the course of medication to determine if a cure has really been obtained.

The most important fact which our discussion has illustrated is therefore that a patient with chronic or recurrent renal infection should have a thorough study of the urinary tract *before* any therapeutic program is determined.





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### DISEASES OF THE BRAIN AND NERVOUS SYSTEM: DIFFERENTIAL DIAGNOSIS AND TREATMENT

#### INTRODUCTION

NEUROLOGY was formerly considered to be a division of medicine which dealt with intricate problems of localization in the nervous system, and contented itself with labeling the patient with the diagnosis of a disease for which there was no effective treatment. Fortunately, this is no longer true, and the treatment for diseases of the nervous system has developed to as high a degree as that for any organ in the body. Advances<sup>1</sup> have been made in the medical therapy of a wide variety of disorders of the nervous system: migraine, epilepsy, Ménière's syndrome, neurosyphilis, acute infections of the meninges, the deficiency diseases, paralysis agitans, narcolepsy, myasthenia gravis and myotonia, to mention only a few. Along with these advances in medical therapy there has been progress in surgery of the nervous system which has resulted in more effective operations for disturbances of the sympathetic nervous system, for the removal of abscesses and some of the tumors of the brain and spinal cord, and for the relief of pain.

In spite of these advances there are still a substantial number of patients with disease of the nervous system for which we have no adequate therapy. Among these are the *heredo-degenerative diseases* of the nervous system, the *virus infec-*

tions (acute anterior poliomyelitis, etc.), the *malignant neoplasms* (gliomas) of the brain, the *muscular atrophies* and *dystrophies*, and *multiple sclerosis*.

Doubtless we will have an effective therapy for many of these conditions in the near future, since the main efforts of workers in this field are no longer directed toward classification and pathologic description, but toward therapy.

The case histories in this clinic are presented to illustrate some of the advances in the diagnosis and treatment of those diseases of the nervous system which are commonly met in a general hospital.

### CASE HISTORIES

**Case I. Meningioma.**—A forty-year-old man, white and married, was admitted to the hospital on March 20, 1940, with a complaint of headaches of three weeks' duration. He had been perfectly well until the onset of these headaches. The pain was most severe in the frontal region, radiating to the occiput. It was present all the time, but varied in severity. The past history and family history were entirely negative.

The general physical examination was essentially normal; the blood pressure was 120/80. On *neurologic examination* the patient was somewhat facetious and did not appear to realize the seriousness of his complaint. The pupils were of normal size and reacted normally to light. The optic disks were choked (about two diopters), with hemorrhages around the edge of the disk. Visual acuity was 20/30 in both eyes and the visual fields were slightly constricted. The left half of the face moved less actively than the right, and there was a slight tremor of the left upper extremity on finger-to-nose test. Sensory examination was entirely normal; the deep reflexes were active in the arms and legs and there was no inequality of the two sides. The abdominal reflexes were not obtained on the left side.

Examination disclosed that the urine was normal, the blood nonprotein nitrogen was 30 mg., the blood sugar was 118 mg., and the serum Hinton test was negative. *x*-Rays of the skull showed no abnormality, and *x*-rays of chest and pelvis were normal. The spinal fluid was under pressure of 270 mm. of water and was very slightly xanthochromic. It contained two lymphocytes per cubic millimeter, and the protein content was 200 mg. per 100 cc. The colloidal gold and Wassermann reactions were negative.

On the basis of the history of headaches and the findings of choked disks, increased intracranial pressure and a high level of protein in the spinal fluid, further investigation seemed justified, and ventriculography was performed. *x*-Ray pictures taken after the air was introduced showed a shift of the ventricular system to the left, with some elevation of the right anterior horn, and at operation a large meningioma was removed from the right temporoparietal region.

The presenting complaint in this patient was *headache*. The severity and constancy of these headaches suggested that the patient was suffering from *increased intracranial pressure*. This hypothesis was further confirmed by the finding of *choked disk*. Although the symptoms were of only a few weeks' duration and there were very few signs of a focal lesion, tumor of the brain seemed to be the most likely cause of this increased intracranial pressure. The preliminary diagnosis was supported by the absence of any evidence of arterial disease or meningeal irritation. The presence of increased intracranial pressure was established by the lumbar puncture, and the high protein<sup>2</sup> content of the cerebrospinal fluid in the absence of a pleocytosis was further evidence in favor of the diagnosis of tumor. The location of the presumed tumor could not be determined from the clinical or laboratory examinations. The slight weakness of the left half of the face and the tremor of the left hand were indications that the tumor was probably in the right frontal lobe, but ventriculography was necessary to establish its exact location and extent.

The finding of a removable meningioma at operation illustrates clearly the danger of trying to make a diagnosis of the histological type of the tumor before operation. The pre-operative diagnosis, on the basis of the short history and the absence of any changes in the skull by x-ray, was glioma of the brain, and therefore carried a very poor prognosis. The finding of a meningioma at operation proved that the preliminary diagnosis and prognosis were entirely wrong. The tumor was removed in toto and the patient is now able to return to work.

**Case II. Lymphocytic Choriomeningitis.**—A twenty-three-year-old Polish woman was perfectly well until November 9th when she experienced a severe frontal headache which lasted for about twenty-four hours. On November 16th the headache recurred with great intensity and necessitated her admission to the hospital the following day.

On admission the patient was acutely ill, somewhat irritable, but well oriented and rational. The temperature was 102° F., the pulse 100 and respiration 20. The general physical and neurologic examinations were entirely negative except for stiffness of the neck, the presence of Kernig's signs, and slight

choking of the optic disks. The urine was normal and examination of the blood was negative except for a moderate leukocytosis.

Lumbar puncture was performed on November 18th. The fluid was under a pressure of 200 mm. of water. It was clear and colorless and contained 6 lymphocytes per cubic millimeter. On the next day the patient's temperature remained elevated and the symptoms increased in severity. At this time the cerebrospinal fluid was under pressure of 250 mm. of water and contained 250 lymphocytes per cubic millimeter. On chemical analysis the fluid was found to contain 58 mg. of sugar and 706 mg. of chloride per 100 cc. No organisms were seen in the stained smear of the centrifuged sediment and cultures were sterile.

The patient remained acutely ill for the next two weeks, with a temperature ranging between 102° to 104° F., finally falling by lysis on December 1st. During this time the meningeal signs persisted, the optic disks became more swollen, and bilateral sixth nerve weakness was noted.

TABLE 1  
THE CEREBROSPINAL FLUID FINDINGS IN CASE II\*

Date.	I. P.	Cells.	T. P.	Sugar.	Chloride.
11/18	200	6 lymphs.			
11/19	250	250 "	...	58	706
11/21	250	700 "	...	56	680
11/23	310	970 "	108	29	677
11/25	260	890 "	106	36	652
11/27	290	1034 "	70	38	654
11/29	0	1095 "	94	46	705
12/ 4	40	210 "	86	32	701
12/ 8	80	190 "	49	44	707
1/27	120	7 "	17	55	725

\* The colloidal gold and Wassermann tests were negative in all fluids. No organisms were found in stained smears and cultures were sterile.

Spinal punctures were performed daily and the findings are shown in Table 1. The pressure remained high until about the 28th of December, after which it fell to normal. The cell count increased until it reached over 1000 cells (all lymphocytes) on the 27th of November, and after this date it began to fall. Coincident with the decrease in intracranial pressure and the number of cells in the cerebrospinal fluid, the patient began to improve. The headaches and the weakness of the sixth nerves disappeared, and the swelling of the optic disks subsided.

On the 18th of December, approximately one month from the onset of symptoms, the patient was discharged from the hospital. She returned on January 27, 1940, for a repeat examination of the cerebrospinal fluid. During the interval she had been at home and had been feeling well. The neurologic examination was entirely negative. The cerebrospinal fluid was under normal pressure and contained 7 white cells per cubic millimeter. The patient was allowed to return to work and has remained well since.

**Case III. Lymphocytic Choriomeningitis (?)**.—A thirty-year-old Negro woman, a laundry worker, was admitted to the hospital on January 20, 1940, with a complaint of headache and vomiting. The headaches began one week before entry and had increased in severity until two days before entry, when she began to vomit and stiffness of the neck was noted. The headache was so severe that she was unable to sleep at night. In addition, she became lethargic and semistuporous and had been unable to retain any food for the thirty-six hours before admission to the hospital.

The general physical examination was negative; the blood pressure was 100/70. On *neurologic examination*, marked stiffness of the neck and bilateral Kernig's signs were noted, and the deep reflexes were all absent. The urine was normal, the blood hemoglobin content was 50 per cent, the red blood count was 3,700,000 and white blood count 11,000, and x-rays of the chest were negative.

The cerebrospinal fluid was under pressure of 500 mm. and was ground-glass in appearance. It contained 315 cells per cubic millimeter, which were all lymphocytes; the protein was 55 mg., sugar 62 mg. and chloride 712 mg.

TABLE 2  
THE CEREBROSPINAL FLUID FINDINGS IN CASE III\*

Date.	L. P.	Cells.	T. P.	Sugar.	Chloride.
1/20	500	315 lymphs.	55	62	712
1/21	240	330 "	33	58	723
1/22	220	154 "	17	52	695
1/24	230	132 "	22	50	704
1/29	150	35 "	17	61	729
2/ 2	150	7 "	11	54	740

\* The colloidal gold and Wassermann tests were negative in all fluids. No organisms were found in stained smears and cultures were sterile.

per 100 cc.; the colloidal gold and Wassermann tests were negative. No organisms were found in stained smears of the centrifuged sediment, and cultures of the fluid were sterile. Because of the high pressure, puncture was repeated on the patient at frequent intervals for the next few days and the findings are shown in Table 2.

The patient's temperature varied between 100° and 101° F. the first few days in the hospital, after which it returned to normal. Coincident with the fall in temperature and with the return of the intracranial pressure to normal, there was a striking improvement in the patient's condition. The stiffness of the neck disappeared, the patient became more alert, and the deep reflexes returned. She was discharged from the hospital on February 4, 1940, three weeks after the onset of symptoms, entirely relieved of all of her symptoms.

*Comment on Cases II and III.*—Both of these patients presented a very interesting diagnostic problem at the time of

their entry to the hospital. The presenting complaint in both cases was *headache*. The nature of these headaches was indicative of *increased intracranial pressure* and the presence of *stiffness of the neck* and *Kernig's signs* suggested that this increased pressure was associated with a meningeal inflammation rather than an expanding lesion. This impression was confirmed by the examination of the cerebrospinal fluid.

The diagnoses considered at this time were: (1) tuberculous meningitis, (2) syphilitic meningitis, and (3) benign lymphocytic choriomeningitis. *Syphilitic meningitis* was excluded very soon by the absence of a history of syphilis and by the negative blood and cerebrospinal fluid Wassermann tests in both cases. *Tuberculous meningitis* was excluded in Case III by the fact that there was never any reduction in the sugar or chloride content of the fluid. In addition, all of the cells present in the fluid of these patients were lymphocytes. While it is common for lymphocytes to predominate in the cerebrospinal fluid of patients with tuberculous meningitis, a small percentage of polymorphonuclear leukocytes is practically always found. In Case II the diagnosis of tuberculous meningitis was entertained for quite a few days because the sugar content was somewhat decreased\* and there was also a moderate reduction in the chloride content of the fluid. This diagnosis seemed less likely, however, when we were unable to obtain any organisms in stained smears of the fluid and the patient began to improve. In neither of these patients was there any evidence of tuberculosis elsewhere in the body, and inoculations of guinea-pigs with the cerebrospinal fluids were negative; consequently the diagnosis of tuberculous meningitis was discarded in both cases.

The diagnosis of lymphocytic choriomeningitis was established in Case II by tests performed by the U. S. Public Health Service in Washington, D. C., which showed that the patient's serum contained antibodies against the virus of lymphocytic choriomeningitis. This test was also performed in Case III

\* The reduction in the sugar content of the fluid from this patient was similar to that in the case reported by Skogland and Baker.<sup>5</sup>

but the report has not as yet been obtained. The clinical course and the evolution of the changes in the cerebrospinal fluid were so typical of lymphocytic choriomeningitis that there is little doubt as to the final diagnosis.

This disease is due to a filtrable virus<sup>4</sup> which can be grown on the chorionic membrane of the chick embryo. The disease in man<sup>5</sup> is characterized by symptoms and signs of meningitis, with lymphocytes constituting 100 per cent, or almost 100 per cent, of the cells in the inflammatory reaction. The disease is only rarely fatal,<sup>6</sup> and complete recovery in a few days or weeks is the rule. Antibodies to the virus appear in the serum soon after the onset of the disease, and are usually present in sufficient quantity for diagnostic testing one to two months after the onset. There is no specific treatment for the infection. The meningeal symptoms and the headaches can be controlled by the removal of cerebrospinal fluid at appropriate intervals.

**Case IV. Early Dementia Paralytica.**—A forty-two-year-old white man was referred to the hospital with the complaint that he had been feeling weak for the past year. There had been some impairment of his ability to drive his automobile, and his friends had noticed a change in his personality in that he did not get along with people as well as formerly and that minor things upset him and made him "fly off the handle." He had been able to carry on his work as a salesman during the past year, but his productive ability had fallen off so greatly that he had done very little work in the past month or two. In addition to these complaints, the patient had noticed that in the past few months he had difficulty in walking in the dark, and that he occasionally stumbled without adequate cause. He suffered from occasional lightning-like pains in the legs and abdomen. The patient had been in good health up until the time of onset of the present symptoms and there was no history of primary or secondary syphilis.

The general physical examination was entirely negative. On *neurologic examination* the pupils were found to be slightly irregular and unequal but they reacted readily to light and accommodation. There was some tremor of the mouth, tongue and extended hand, and a slight difficulty in repeating test phrases. The knee and ankle jerks were absent and there was a mild degree of impairment of the vibratory sense in the lower extremity. The Romberg test was positive. Mental examination revealed the patient as somewhat anxious and disturbed. His memory for recent and for remote events showed a slight degree of impairment. The blood Hinton test was positive. The cerebrospinal fluid was under normal pressure and contained 44 lymphocytes





discharged from the hospital in care of his family physician. He has returned to work and is receiving weekly injections of tryparsamide.

The symptoms in this patient were those of *cerebral involvement* (failing of intellectual capacities and changes in personality), together with symptoms of involvement of the spinal cord in the nature of *ataxia* at night and *lightning pains* in the lower extremity. The cerebral symptoms are considered to be classical for early dementia paralytica, and this diagnosis was confirmed by the results of the examination of the blood and cerebrospinal fluid. With the spinal cord symptoms and signs this patient would be classified as a taboparetic.

Since the patient was almost incapacitated for productive work, it was thought advisable that he be treated<sup>7</sup> with malaria fever at once, and that this treatment be followed by weekly injection of tryparsamide after discharge from the hospital. He remained in the hospital approximately one month and, during this time, there was an improvement in his mental state. Since his discharge from the hospital he has returned to work, and is receiving weekly injections of tryparsamide from his family physician.

The *prognosis* in this case is good since the diagnosis was established before there was evidence of extensive damage to the brain. The process in the central nervous system has been checked by the malaria treatment and should be eradicated by future treatments with tryparsamide. The duration of these treatments with tryparsamide must be governed by examinations of the cerebrospinal fluid at intervals of from six to eight months but it is quite probable that he will need treatment for at least two to four years. He should, however, in the meantime be perfectly capable of carrying on his work as a salesman.

**Case V. Parkinsonism.**—A fifty-year-old white mechanic was admitted to the hospital on April 17, 1940, complaining of tremor in the upper extremities of three years' duration. The patient had been perfectly well until three years ago when he began to notice tremors in the fingers of the left hand. These tremors gradually spread to involve the whole hand and the forearm. In the last year the right hand and arm were similarly affected,

In addition, the patient complained of generalized stiffness of the muscles, dragging of the feet, and pain in his right shoulder. He had slowed up in all of his activities and had not been able to perform his work as loom-fixer for the prior three months. The tremors tended to increase when the patient was excited and disappear when he was asleep. The past history was not significant. The patient had never had influenza or sleeping sickness.

On examination he was found to be mentally alert, well oriented, cooperative and intelligent. Findings of the general physical examination were within normal limits. On *neurologic examination* his face was seen to be expressionless, with infrequent blinking of the eyes; his gait was slow with some shuffling of the feet; his posture was stooped; his arms were held abducted from the side and slightly flexed at the elbow and wrist. There was a rhythmic tremor of both hands of sufficient amplitude to keep the arms in constant motion. The tremor disappeared for a period of ten to twelve seconds when the patient stretched out his arms or when he performed any voluntary movement of the upper extremity. There was cog-wheel rigidity of the upper extremity. The neurologic examination was otherwise negative.

The patient was started on treatment with extract of belladonna, 2 pills a day, each pill containing 0.4 mg. of total alkaloid. This was gradually increased to 4 pills a day, at which time the patient experienced some dryness of the mouth but there was complete cessation of all tremor. He felt much better and could move around faster and was discharged from the hospital with instructions to take 5 tablets (2 mg.) of the extract of belladonna root daily.

The symptoms in this patient—*tremor* and *rigidity of muscles*—are characteristic of parkinsonism. These symptoms are due to degenerative changes in the basal ganglia, particularly the substantia nigra. In the absence of history of any acute inflammatory process or other causes of lesions in these nuclei, it must be assumed that the changes were due to diffuse arterial disease.

Although symptoms had been present for three years, the patient had not received any systematic treatment. He stated that he had been given some pills which did not relieve his symptoms, and which he had ceased to take. If this medicine was one of the belladonna alkaloids it had not been given in amount sufficient to produce dryness of the mouth.

Treatment with the *belladonna alkaloids* (stramonium, hyoscine, atropine, etc.) is attended with a variable degree of success in these cases. Improvement of some degree is noted in practically all instances and in some the results are re-

markable. Stiffness of the muscles, salivation and pains in the extremities usually respond more readily to treatment than do the tremors. It is important that the belladonna alkaloids be given in dosages sufficient to control the symptoms, but the best results are obtained when the therapeutic dose is below the level which produces toxic side-reactions. The most common toxic symptoms from overdosage of belladonna are excessive dryness of the mouth, difficulty in reading, difficulty in urinating, and gastro-intestinal complaints (dysphagia, diarrhea). In the treatment of patients with parkinsonism of the arteriosclerotic or postencephalitic type, the initial dose of the belladonna preparation (stramonium, hyoscine, atropine, etc.) should be small and gradually increased until symptoms are relieved or toxic signs develop. Amphetamine (benzedrine) sulfate<sup>8</sup> in doses of 10 to 40 mg. daily is often of value when used in conjunction with the belladonna alkaloids.

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## CLINIC OF DRS. MERRILL MOORE AND JOHN ADAMS ABBOTT

FROM THE PRIVATE PSYCHIATRIC CLINIC OF DRS. MOORE AND  
ABBOTT

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### DIFFERENTIAL DIAGNOSIS OF NEUROSES AND PSYCHOSES

You have asked us to discuss the differential diagnosis between neurosis and psychosis. Your reason for requesting this discussion became more apparent to us when we turned to the literature on the subject, for there we found very little that could be placed under this specific heading. The standard textbooks deal with the subject only rather incidentally. A search through ten volumes of the Quarterly Cumulative Index Medicus elicited only two titles which referred explicitly to this problem. One,<sup>6</sup> alas, is in Dutch and was therefore largely incomprehensible to us. The other<sup>7</sup> was an important paper which gave the backing of authority to some of our own views. This latter article, by Dr. Jacob Kasanin, Director of the Department of Psychiatry of the Michael Reese Hospital in Chicago, also contained important references relevant to this subject.

Before going on to the case presentations which you have requested, we would like to say a few introductory words.

**Steps in Differential Diagnosis.**—THE PSYCHOSES.—The *first step* in the differential diagnosis between neurosis and psychosis is the simple decision as to whether the individual can care for himself or, because he talks and behaves so strangely, must be restrained or cared for by others. Com-

monly this decision is made by the layman and made by him correctly. If the individual does behave so strangely that he must be restrained or cared for by others, then he very probably does have a psychosis. Otherwise he probably has a neurosis.\*

The *second step* in the differential diagnosis between these two conditions is the more difficult one of deciding whether the particular individual's disturbance should or should not be called a "psychosis" on the basis of its resemblance to one or more among several types of disturbance conventionally agreed to be psychoses. The particular individual's disturbance is a psychosis if, in the opinion of experienced observers, it does closely enough resemble one or more among the several types of disturbance conventionally agreed to be psychoses. Otherwise, again, it is probably a neurosis.\*

Those syndromes or types of disturbance which are conventionally agreed to be psychoses may be enumerated, on generally accepted authority, as follows:

1. The *organic psychoses* (arteriosclerotic, paretic and other types), which (on account of their familiarity to most physicians) need not be further considered in this presentation, and

2. The *functional psychoses*, which are schizophrenia (also called *dementia praecox*), *paranoia*, manic-depressive insanity, and the other severe depressions usually called "agitated depression" and "involutional melancholia."

THE NEUROSES.—*Pari passu* with the two steps already described, which serve primarily to establish or exclude psychosis, one is also seeking *positive* rather than merely negative evidence of neurosis. One's progress toward this end, too, may be described in two steps:

Of these two steps the *first*, again, is taken almost as well by the layman as by the physician and consists in deciding whether or not the individual's way of thinking entails, for himself or for those with whom he associates, an appreciable

\* We refer here, obviously, to those who have mental problems and not to so-called "normal" persons.

degree of suffering that could be avoided if he thought differently. If it is decided that the individual's way of thinking\* does entail, for himself or for those with whom he associates, an appreciable degree of suffering that could be avoided if he thought differently, then he may be considered neurotic or may be judged to have a neurosis. ("Neurosis" and "psychoneurosis" are here used synonymously, as are the corresponding adjectives "neurotic" and "psychoneurotic.")

The *second step* in establishing the positive diagnosis of psychoneurosis is the more difficult one of determining the presence or absence of organic pathology and of eliciting signs or symptoms, or demonstrating or reconstructing psychodynamic processes (symptoms related to wishes, motives and experiences) which are similar to the signs, symptoms, or psychodynamic processes known to have occurred in extensively studied cases which answer to the definition of neurosis and which present a number of predominant syndromes upon which there is fairly general agreement. It should be noted that the agreement on these syndromes seems to be less general than the agreement upon the psychotic syndromes.

**Neurotic Syndromes.**—These neurotic syndromes may be somewhat tentatively enumerated as follows:

1. The *organic neuroses*, or actual neuroses: a highly debatable group of which neurasthenia is the only one that even comes near to getting a majority vote among psychiatrists, and
2. The *neuroses* (or *psychoneuroses*), or conditions which are generally agreed to be results primarily of the way the individual thinks.

We offer the following list of commonly recognized neurotic syndromes: *hysteria* (conversion hysteria), *anxiety neurosis* ("anxiety hysteria"), *compulsion neurosis*, *hypochondriasis*, *character neurosis*, *psychopathic personality*, and *psychoneurosis of mixed type*, with special symptoms such as anxiety, alcoholism, feelings of unreality, psychic impotence, or other peculiar psychoneurotic symptoms which occur with-

\* And some might add: "and behaving."



out sufficient associated evidence to indicate one of the preceding better defined syndromes.

**Guiding Points in the Differential Diagnosis of the Neuroses from the Psychoses.**—As guiding points in the differential diagnosis of neurosis and psychosis one should have definitions of the two terms:

The following definition of neurosis is quoted from the glossary to "Facts and Theories of Psychoanalysis" by Dr. Ives Hendrick<sup>1</sup>: "*Psychoneurosis* (colloquially, 'neurosis') . . . is a disturbance of psychological or physiological functions, of the general personality, or the social adjustment, without conspicuous evidence of psychosis or emotional indifference to other people, caused by unconscious conflict, and productive directly or indirectly of a significant limitation of pleasure or success, or a significant degree of psychic or social suffering."\* To this, one should add, for emphasis, *without demonstrable "organic" cause*.†

And this next definition is one that we offer on our own responsibility: A *psychosis* is such thinking and feeling as give rise to mutism or speech and other behavior that (especially in the opinion of experienced observers) closely resembles one or more among several types of behavior which have been generalized from scientific observation on those adult hospital patients who were members of our Western European culture, and who behaved in a way that endangered their own physical welfare (or that of themselves and their fellows in this culture) and who were therefore restrained and cared for by their

\* One of us (J.A.A.) roughly summarizes this definition in the jingle:

"Who is neurotic?  
The person who borrows  
Or visits on others  
Avoidable sorrows."

† There are many worthy authorities who would disagree with this statement. On the one hand there are those who would hold that a neurosis is by definition a non-organically produced emotional disturbance; and on the other hand there are those who would claim that a neurosis is a manifestation of constitutional inferiority, or the symptom of a basic though possibly obscure organically produced dysfunction. Midway between these viewpoints is the "psychosomatic" or "psychobiologic" point of view.

fellows in this culture; and who, because of the danger to themselves (as distinguished from their fellows) were judged by their fellows as being not responsible for (and therefore not criminal in) their behavior. The types of behavior that have been generalized on the principles stated in this rather cumbersome definition are those syndromes already enumerated as the types of disturbance which are conventionally called psychoses.\*

Finally to *summarize* and to augment what has already been said: In the case of a particular individual, the differential diagnosis between neurosis and psychosis is the expert decision as to whether or not the picture or syndrome of the individual's thinking, feeling, and resultant activity is closely similar to certain syndromes conventionally called "neuroses" or to certain syndromes conventionally called "psychoses." In many cases the decision can be made without difficulty and will be a matter of general agreement among experts. In some other cases, the decision either cannot be made, or if it is made will be a matter of general dispute among experts. No *qualitative* difference between neurosis and psychosis has been demonstrated and generally agreed upon. The difference between neurosis and psychosis seems to be a *quantitative* one (or "a matter of degree") with intermediate conditions† that cannot be assigned to either category. Furthermore, at different times in his life a single individual may have a neurosis, or a psychosis, or a condition that is intermediate between neurosis and psychosis.

**Characteristics of the Various Syndromes.—PSYCHOTIC.**—We may now very briefly characterize each of the syndromes named above:

\* The commonest *symptoms* of psychosis are great extremes in mood, severe disturbances of activity and speech, delusions and hallucinations, gross memory disturbances (excepting amnesia), lack of insight, disorientation, confusion and marked disturbances of judgment, gross disturbances in social adjustment and interpersonal relationships, marked personality changes, and deterioration of character. Generally speaking these symptoms do not occur in the neuroses. It is our hope that the definition we have attempted to give to some extent reconciles the medical and the several legal definitions of psychosis or insanity.

† These are the so-called *borderline conditions*.

In the *organic psychoses* there may be more or less gross disturbance in any or all those psychobiological functions described in the familiar mental-status outline. Different disturbances are characteristic for different disorders, but these differences need not be considered here. Typically the headings of the mental-status outline are as follows: General behavior; stream of talk; mood; dominant preoccupations, including notably misinterpretations, delusions, illusions, and hallucinations; orientation; memory, ability to calculate, and grasp of general information; judgment; insight (does the patient realize that he is mentally disturbed).

To proceed with the characterizations of the *functional psychoses*:

In *schizophrenia*, the patient's feelings, behavior, and thought are all disordered, and his attention is commonly withdrawn from the environment.

In *paranoia*, the patient's intellect is intact, but his reason is largely prostituted to proving as true his delusions of being unfairly treated and persecuted.

In the manic phase of *manic-depressive insanity*, the patient is elated and is very active, mentally and physically, and may indulge in "flights of ideas." In the depressed phase of manic-depressive insanity there is depression, difficulty in thinking, and slowing of thought and physical activity.

In *involutional melancholia*, the patient is typically about fifty years old, is depressed without being slowed up, feels anxiety, has feelings of unreality, and has hypochondriacal or nihilistic delusions.

In the *agitated depressions*, the picture is very similar but there is a greater degree of physical activity. The patient may be destructive or aimlessly overactive.

NEUROTIC.—To give now some thumbnail sketches of the neuroses: The *neurasthenic* is typically deficient in energy, preoccupied with physical complaints, and complaints directed against things and people in the environment.

The *hysterics* are predominantly volatile people, warm and charming in their social contacts, either not apparently highly

aggressive, or, if they are aggressive, they do not recognize their aggression consciously.

The *conversion hysteric* has the kind of signs and symptoms that can be induced typically by the use of hypnosis.

In *anxiety hysteria*, the person of the temperament which has been described as "hysterical" feels keen anxiety which is often attached to specific situations such as going into crowds.

The *compulsion neurosis* is characterized by compulsions (for example, having to step on each crack of the sidewalk), obsessions (for instance, having to think certain words over and over again), and generally ritualistic behavior (making elaborate schedules, for example). Often a true compulsion neurosis develops in an individual with an abundance of manifest aggression and a conscious recognition of this aggression far exceeding the hysteric's recognition of his or her aggression.

*Hypochondriasis* is characterized by bizarre bodily sensations. For the patient, these sensations are the object of concern or of an anxiety that is ruminative, as contrasted with the volatile anxiety of the *hysteric*. Temperamentally the *hypochondriac* is not so warm and friendly as the *hysteric* and is more ambivalent (that is at once positive and negative) in his attitude toward others. The compulsion neurotics vary in temperament between the hysterics and hypochondriacs.

A *character neurosis* is one in which the trouble-making thinking and activity are not rejected by the individual in whom they occur as alien to himself but are defended by him as part of his cherished personality.

The *psychopathic personality* is one who, without any other characteristic disorder, appears to be unguided by the ordinary dictates of conscience and personal responsibility to others.

The diagnostic group "*psychoneurosis of mixed type*" is a convenient catch-all for the greater part of those disturbed individuals who cannot be fitted into the preceding categories.

We have chosen in these characterizations to approximate the irreducible minimum of psychiatric description rather than

to go even part way in the direction of that descriptive proximity to which psychiatry is prone, for which there are many real justifications, but for which, alas, there can apparently be no definite terminus (other than the death of the last describing psychiatrist). It would seem possible to regard the specific clinical pictures of descriptive psychiatry largely as blendings and elaborations of the syndromes here given minimal characterizations. Without any hope of perfect success, we have attempted in these minimal descriptions to give the essential basis of agreement among the many minds that today observe the problems of psychiatry and inherit the traditions of yesterday's observers. In this attempt we have accepted, for our guidance, present-day good usage as it is reflected in such a standard text as that by Henderson and Gillespie<sup>2</sup> and we have utilized the terminology and attitude that prevail in such clinics as the Psychiatric Service of the Massachusetts General Hospital and the Neurological Service of the Boston City Hospital. Excellent signposts are available in medical libraries where recent volumes, such as the Cabot-Adams<sup>3</sup> "Physical Diagnosis" and (prominent among the psychoanalytic summaries) "Facts and Theories of Psychoanalysis" by Dr. Ives Hendrick.<sup>1</sup>

We wish to be the first to call attention to one among the many defects in this attempt: we have not tried to discuss "traumatic neurosis," especially as this subject has been so well and so recently dealt with previously in the *MEDICAL CLINICS OF NORTH AMERICA*.<sup>4</sup>

**Diagnostic Procedures.**—The diagnostic procedures of psychiatry differ from those of medicine and surgery only in *emphasis* and in a limited use of *formal mental tests* such as the Stanford-Binet and Bellevue (Wechsler) Mental-Age Tests and the Rorschack Test. Psychiatry places much more emphasis than do the other branches of medicine on observation of the patient's *behavior*, attention to his *thoughts*, *feelings*, and *life history*, and the observations and opinions of those *who "know" him*.

The psychiatric observation of the patient is given guidance and form by bearing in mind the familiar *mental-status outline*. One excellent example of this is described very well by Monrad-Krohn.<sup>5</sup> Henderson and Gillespie<sup>2</sup> also have given a useful outline for these examinations as well as Cabot and Adams.

There are no *laboratory* procedures for distinguishing between neurosis and psychosis.

The differential diagnosis between neurosis and psychosis, as has been said, differs in many ways from diagnosis in the other branches of medicine. In psychiatry, not only is there greater emphasis on the *personal* equation, but accordingly, less possibility for diagnostic precision, the diagnostic terms generally indicating categories of behavior (rather than etiologically precise disease entities). It is likewise possible to choose between an *indefinite* number of diagnostic categories (almost as many categories as there are patients) or some such restricted number as was given in the preceding paragraphs.

The lesser possibility of diagnostic precision makes it almost necessary to acknowledge what might be called a principle of *diagnostic approximation*: the principle, that is, that in many cases the individual's syndrome approximates rather than exactly reproduces an idealized picture of, let us say, "pure" conversion hysteria or "pure" schizophrenia. Indeed, the exact diagnosis achieved in other branches of medicine seems to be regularly achieved in psychiatry only when one establishes an *organic* basis for the mental symptoms: a basis, for instance, such as syphilis, which gave precise delimitation to the picture of general paresis, or frontal lobe tumor, or bromide intoxication.

In order to illustrate the differences we have outlined as existing between cases of neurosis and cases of psychosis, we wish to present briefly the histories of the following patients whom we have recently studied and treated. The cases in this presentation are necessarily condensed. Only the salient points in diagnosis and differential diagnosis are presented.

## ILLUSTRATIVE CASES

**Case I. Schizophrenia.**—This patient (Miss M. I.) is a twenty-three-year-old society girl, known to her friends as "Mimi." She has become mentally very much disturbed while spending the summer with her mother at a camp in the Adirondacks. It is decided, after some deliberation, that the best way to manage her problem will be to drive her by automobile to a sanatorium in the vicinity of Boston. Her physician, who is a friend of the family, will accompany her and her mother on this trip. The physician gives the following account of this journey:

"Mimi was withdrawn, turned away, had her face down and her hat over her face. She was an asthenic, stringy blonde, drably disheveled in a shapelessly hanging suit of a faded powder blue. She didn't talk much, grimaced and laughed inappropriately to herself, slyly. She got in and out of the car as if she were tired. She sat in the back seat and tore up some old rags she found and threw them out on the road. She also tore newspapers. She continued to grimace, to make inappropriate remarks, and laughed to herself. She took a knitting bag and put it over her head; then she put it over her face and later put her head into her mother's purse. She took off her shoes and tried to throw them out the window but was prevented from doing so. She unpacked her bag in a disheveled way. She would not urinate during the entire day though asked to do so. When they stopped for lunch in the middle of the day, her behavior was interesting: She refused to get out of the car and, when she did, she was physically erotic with her doctor; she pushed her body against his and hugged him in front of people on the porch of a restaurant. She appeared to pay no attention to them but seemed aware of her mother and the nurse. In the restaurant, she was childish and irritable. She would snatch things off the table and throw dishes on the floor. She did this in a childish manner as if she wanted to be dominated. Her doctor made her put them back, which she did. She created a little furor at the time she was urged to go to the toilet: She would not go. She was hot and sweaty. She did not speak, drooped over the table, did not eat her soup, ate like an animal, and seemed fatigued and tired. She did sly things to irritate her mother. She would jerk the table cover off and upset things; so it was decided that she was too disturbed to stay in the restaurant. Back in the car again, she took off her shoes and rummaged in her bag in a vague way, throwing the contents all over the car. They arrived at the sanatorium at 6 o'clock. She was tired and was taken by the attendant who persuaded her to urinate for the first time that day. Mimi had been negativistic all through the trip, putting clothes and hat on backward repeatedly. She refused to do anything. Nothing pleased her, and she didn't want to do anything when ordered. She had little to say, laughed a great deal, and continued to grimace."

Seven weeks later the doctor in charge of her at the sanatorium wrote saying, "Mimi hasn't changed much yet. She occasionally has a few good days when she is sociable and more interested and associates with other persons and likes to take part in games and conversations. Then, unfortunately, after two or three days, she relapses into a state of apathy."

This patient was obviously psychotic. Her behavior and manner were so strange that her mental illness was apparent to all who saw her. She was strikingly withdrawn and bizarre in her general deportment and had ceased to communicate with or respond to those around her. She illustrates the extreme type of behavior and thinking disorder described as "schizophrenia." Her apathy or inappropriate moods corroborate this diagnosis. No one, not even a child, could fail to observe and be aware of her disturbance. In this case there are few if any symptoms of neurosis, as commonly considered. The crudity of her expression and the disorganization of her personality speak for themselves.

**Case II. Manic-depressive Insanity.**—Mr. K. H. This case is presented as the picture of a *manic episode* in a patient on whom we make the following diagnoses: *manic-depressive insanity*, psychopathic personality, drug addiction (alcohol, coal-tar drugs), homosexuality. The homosexuality is grossly manifest only during manic or drunken episodes. At other times it is repugnant to him and is repressed. He has been under care for four years. We first saw him at the age of twenty two.

When neither manic nor intoxicated this patient is "intelligent, immature, very attractive, socially well mannered, and somewhat effeminate." He is a handsome boy, over six feet in height, about 170 pounds in weight.

He is first seen by one of us in his mother's house. He is wrapped up in a blanket on a couch downstairs. He is overactive, overtalkative, and sometimes bursts out in anger and criticism toward his mother, who is trying to care for him. The night before he did not get to sleep until 5 A. M., and he ate a large meal at midnight. In a preliminary contact over the telephone, speaking to us at his mother's request, he said: "The family are worried about me. I don't think it is so serious." His voice at that time sounded somewhat high, elated, agitated. He is later to give some account of his immediate present illness, saying that "The joy of life" culminated in a sudden "ego-



maximation," since when he has been drinking and running around a little (his own estimation), has been proud to appear with his lovers, his thoughts have been "beautiful," he has been amused, interested in everything, has realized that he could drop in anywhere, has used the telephone a lot, has thought of going to London, and has asked his mother to give him his bonds so that he could sell them in order to finance the trip.

On the second day of our contact with him, in the company of a suitable companion, he leaves by automobile for a remote sanatorium in the country. During the drive he is elated and verbose. He talks about New York. He becomes hungry. A stop is made at a drug store for a light lunch. In the drug store he tries to call New York on a pay telephone without depositing any money. The trip is resumed. They stop again for dinner: In the dining room he sends his calling card to an unknown girl with a written request for some polish remover (before leaving home he has painted one of his fingernails a brilliant red), and she returns the card, saying that she has no polish remover. The trip is resumed again. At 11 P. M. they stop for the night at a hotel. In the lobby he talks loudly; at 11:30 he goes to sleep under amytal, but at 1:00 A. M. he is awake again and trying again to make long-distance calls to New York. He is dissuaded from this and says then that he feels hungry and sends for the bellboy. When the latter arrives, our patient exclaims how "nice" he is and makes subtle remarks about "having him," remarks which embarrass the bellboy, much to our patient's delight. He then orders a collation containing cole slaw, several Western sandwiches, ice cream, turkey, roast beef, milk, and some cocktails. His companion persuades him to reduce this to two sandwiches and a bottle of milk; he attempts a few more long-distance calls, and finally, under paraldehyde, sleeps from 2:30 A. M. to 9:00 A. M. At last arriving at the sanatorium, he eats a small lunch, talks incessantly, and then goes for a two-hour hike, during which he rolls about in the snow and dances with much shaking of his hips and shoulders, and, meeting a farm boy on the road, tells him he is sweet. On getting back to the house, he spends two hours at the player piano, playing it loudly, singing, doing suggestive dances, and making gestures of feminine seduction toward another male patient.

These observations are reported from the fourth month of a manic attack which lasted four or five months. For two years preceding this attack he had been subject to definite but less dramatic elations and depressions. There have been no equally dramatic mood swings since the remission of this manic attack. This patient continued to behave much as described above and has been living for several years in a private mental hospital from which he constantly begs to be released "so he can get a job." In the opinion of the physicians in charge he is still too ill to work.

**Case III. Manic-depressive Depression.**—The doctor who refers the patient (Mr. B. T.) says, over the telephone: “. . . He tried to commit suicide. He tried with gas—got dizzy—stopped—fell down . . . . He cried the night before last and yesterday: had a bad day. He is very discouraged.”

The patient himself, on arriving at the office, proves to be a tall, handsome young Jew, twenty-nine years old, not particularly submissive in his appearance. He looks well, has a good “front”; but when he begins to talk, he becomes definitely anxious and begins to look depressed. He talks rather slowly and in a very soft and suffering voice.

He says: “I am always thinking a day ahead and I always worry about things. I have a complete loss of confidence in being able to take things. Whatever I tell you about myself is slipshod. I can't think very straight. I feel all right at times; then at other times this nervous feeling comes over me that I can't describe. I find it hard to concentrate. Yes, very difficult. I know what a damn fool I am; but no matter how I try, my troubles always come pouncing right back. I have been very discouraged lately, so much that I have not had any desire to live. Is this an unusual situation, Doctor, or is it common? I have gone through awful hell. I have given this thing an awful battle. I know I am sick. I have suffered a great deal, none will know how I have suffered. It has been an awful struggle. I want to get well, and yet I feel as if I ought to fight you and the treatment. This is the last resort. Do you think I should be treated?”

His wife says: “He cried this morning and is very discouraged. He told me he had no desire to live and the reason he was living at the moment was that he was a weak person. He refuses food. We received a letter from my sister telling about our children who are staying with her. He wept bitterly and said he had an idea he would never live to see them again. He keeps reading and rereading that letter.”

This is his second severe depression. It developed insidiously and became “bad” three or four months before the patient came to see us. About a week before and again a few hours before coming to the office, he attempted suicide by asphyxiation with the exhaust fumes of his automobile. In the course of two weeks the depression underwent a good but only temporary remission.

Two and a half years ago a daughter was born to him and his wife, and in the ensuing months he went through a week or more of real and deep depression. This was his first severe depression.

About ten years ago, during his last year of high school and his first year of college, he was subject to hypomanic episodes of bolsterousness and argumentativeness which were to him, quite consciously, periods in which he triumphed over his shyness. This item is of interest in view of the theory

that the manic, or in this case, hypomanic reaction is a period of successful overcompensation for anxiety and other painful psychic feelings.

This patient continued under treatment for a short period, then decided he was well enough to travel abroad, which he did with his wife. Their trip was disturbed by the recurrence of some of his symptoms, but he returned to work and has gotten along fairly well and has continued treatment irregularly with a psychiatrist who lives near him and deals with him in a repressive and inspirational way, as opposed to an analytical and interpretive method of handling of his case.

**Case IV. Agitated Depression.**—We first saw the patient (Mrs. N. B.) on March 15, when she was brought to our office by a son and daughter. She was a stocky, busty Jewess, about five feet two inches tall, fitfully combative and, during these fits, mentally out of touch with those about her. At other times she was cooperative but preoccupied. At neck and cuffs she had burst the clasps of her decent, nondescript, black house dress.

She was taken directly from the office to a nursing home. Her psychosis progressed rapidly, became very severe, and then remitted, so that by March 26th she was markedly improved. On April 2nd she described her experience during the height of the psychosis by saying, "My mind was so covered with a number of things that nothing seemed to untangle."

During the height of the psychosis (March 14th to 26th) she was overactive, destructive, combative, dominated by delusions, and required restraint and sedation. The delusional and other preoccupations are well represented by the following notes and quotations: "Call up my father, call up my father. Tell him I have committed murder. It is going to be in the papers." She begs to be placed in restraint so that she will not commit any more murders, believes that the electric chair is going to be her fate, asks for a knife so that she may kill herself. "I swear by the Bible and all the fixings of the synagogue that I committed murder. . . . The whole world is wrong, the world is going to suffer on account of my mistake." She claims that a lot of people are going to be murdered and that she is responsible. She becomes violent, trying to scratch the nurses and shouting, "I'm going to be murdered." She says she has killed one thousand people. She asks who will pay for all the attention which she is receiving and says that her husband hasn't got any money. She is restless and confused, worried about her family, and says, "I didn't do it, I'm not crazy, only I have crazy thoughts." She

keeps repeating. "I'm a crazy woman with a good mind. The children should have told me. . . . I'll get the electric chair. . . . I'm crazy. . . . Dr. R. come to me. Please give me some poison and then everything will be all right." As noted before, this agitation slowly subsided, and after several weeks she returned to her home with an attendant and became superficially, at least, adjusted to her surroundings.

In this case, again, the extreme nature of the symptoms, the agitation and the attitudes of self-accusation, with the delusional material, mark the case unmistakably as a psychosis. The degree of the patient's tension, the severity of her anxiety (if one can call it that) and the total loss of insight during her disturbed period clearly correspond to the well-known clinical picture of *agitated depression*.

**Case V. Conversion Hysteria.**—This patient (Mrs. W. B.) is presented as an example of conversion hysteria with an intercurrent psychosis precipitated by surgical menopause. At the time of entering treatment she was in her middle thirties, and the mother of four children ranging from eight to twelve years of age.

In the course of treatment her smiles endeared her to the office staff and she brought them many dainty presents of her own cookery and needlework. These details were typical manifestations of her personality which was predominantly affectionate and almost never consciously aggressive.

Outstanding among the symptoms for which she entered treatment were: (1) periodic, coarse tremor or, better, waving motions of the left hand and forearm; (2) urinary dysfunction; (3) sharp abdominal pains; (4) "nervousness" and general muscular tension. She was the type of patient who sometimes passes in endless rotation through a succession of out-patient clinics.

Of the foregoing symptoms we will here consider only the urinary dysfunction and some of the data immediately relevant thereto. This dysfunction consisted, in large part, of a tendency to urinate in short, intermittent spurts, and of periods of painful and involuntary urinary retention. Treatment did something to correct this dysfunction.

The tendency to urinate in intermittent spurts had begun at about five years of age, shortly after she had seen a man masturbate and had been impressed by his erected penis and the intermittently spurting seminal ejaculations—apparently, if she could not herself possess the impressive organ, she could at least imitate what, from her observation, was one of its distinctive functions. Further anamnestic work elicited from her the recollection from girlhood (about the age of seven years) of putting her hand over the lower

abdomen during painful and apparently involuntary urinary retention and thinking in the back of her mind, "Well, thank goodness, there is something there, anyhow"—the something being in reality a painfully full bladder and, in fantasy, a full womb. Two themes, the desire to have a penis and the desire to be pregnant, had dominated her life from early years; and the preceding sentences indicate their relation to the urinary dysfunction. The urinary dysfunction was very carefully studied from a physiological point of view before psychotherapy began, and the negative findings accumulated then, plus such positive psychologic evidence as that just cited, indicated that the urinary dysfunction was a pure conversion symptom.

In the second year of treatment it was interrupted to permit the patient to undergo a laparotomy for the removal of a fibroid uterus. When she came back to resume treatment, she told the following story: She had undergone the operation in the belief that the fibroids would be removed without the removal of the uterus or other organs. Her postoperative convalescence had progressed well until about the second day, when she learned that a complete hysterectomy had been performed. This information upset her very much, and she developed, apparently within the day of learning it, a distressing conviction that she was different from other women in that she possessed a penis. This conviction that she possessed a penis was so strong and the distress occasioned by this conviction was so great that she would not permit exposure of the genital region, and she successfully maintained this attitude, to the inconvenience of the nurses who were caring for her. On being discharged home, she neglected her housework and found herself able only to sit for long hours listening to the radio.

On finally returning to treatment, the belief that she possessed a penis, albeit what had now become an "inward penis," still tormented her. She came to believe that a venous varix in the vicinity of the clitoris was the glans of this "inward" organ. During the ensuing years of treatment this belief faded and she was released from the torment which it occasioned her. At the same time she came to a progressively clearer recollection and appreciation of the positive childhood desire to have a penis and to be a boy.

It is upon the events related in the two preceding paragraphs that we have based our use of the term "intercurrent psychosis." Mrs. W. B. thus exemplifies the occurrence at different times, in the same individual, of neurosis (conversion hysteria) and psychosis. Probably the psychosis could be classified as a *transitory involutinal melancholia*. In this patient the inward symptoms would never have been evident to an outsider. Only a few of her symptoms were ever vocal. Only her strange behavior and manner were obvious. She would have been singled out of a group as a stiff, prim, reserved or timid woman. Her psychotic episodes were ephemeral.

**Case VI. Anxiety Hysteria.**—Bertram (Mr. B. V.) is a twenty-three-year-old law student who, throughout his fifteen-hour-long therapeutic interviews, displays a personality warm, boyishly exuberant, and combative but with disarming charm. His letters home reveal an excellent relationship between himself and his "folks": he gives his father a verbal slap on the back and calls him "fellow"; towards his sister he maintains the pose of a patronizing, sarcastic-affectionate older brother, who really is always affectionate toward her.

Hidden within this personality rages the neurosis. He has come for treatment because of self-obtruding ideas and fears which have made it "almost unbearable to sit in class."

The immediate present illness began suddenly two years and some months before coming to us. The onset occurred while the patient was in class listening to the professor lecture on the subject of, "What is an act?" In connection with this question, the professor said that an act was something which you willed. The patient was suddenly seized with an attack of anxiety and became preoccupied with the idea that his mind was something material, a gray body inside his head, acting independently of his will—"something working inside your head like a foreign mechanism." This self-obtruding and alarming preoccupation continued to trouble him, and his anxiety was reinforced by reading about an insane man who believed that he had, not a foreign mechanism, but a canary in his head.

Since the preceding episode, he has been subject to phobias of which we will give the following partial account: In classrooms and on one occasion in a courtroom where the door was locked, he has experienced definite claustrophobia. In connection with the classroom episodes, he described "a fear that if I am not near the door, it will accentuate the nervousness so that I would have to leave the class." He accordingly always either takes a seat near the door or, if such a seat is not available, finds some pretext whereby he can justify to others his sitting on the floor near the door. With regard to the courtroom episode, he says that, while the judge was charging the jury, the doors of the courtroom were locked and he felt a great deal of anxiety about not being able to get out—anxiety which he quieted by a number of minor distracting activities and which he strove successfully to conceal from the friend who was attending the trial with him. Since hearing about a subway accident in which the eighth car of the train was most seriously damaged, he has had a fear when traveling in the subway of a similar accident, and he has met this fear by an aggressive effort to master it by riding in the ninth car. When riding in a street car, he will have a fear that the car will jump the track or have some other mishap, and he will quiet this fear by locating the lever by which he could open the door in case of an emergency. Once, during

a visit to New York, he was obliged to occupy a bedroom several floors above the street, and he had the fear of walking out the window at night in his sleep. To quiet this fear he placed a dress suitcase on the floor between his bed and the window, with the hope that, if he did walk in his sleep, he would be wakened by stumbling over the dress suitcase. In the railroad train he will have fears of the brakeroads snapping or of some other mishap occurring.

His symptoms remitted rapidly under treatment. A variety of factors led him to elect a repressive rather than a radically analytic solution of his problems.

Meeting this patient socially, one would not be able to detect his anxiety. During treatment it drained from him freely. The deep unreasonableness of his fears was impressive, even though most of the time he had considerable insight, was in excellent contact with his surroundings, and socially got along very well.

#### **Case VII. Obsessional (or Compulsion) Neurosis.—**

The obsession takes the form of doubting and the compulsion takes the form of investigating, verifying and rechecking in order to quiet the doubt.

The patient (Mr. T. G.) is a young married man, short, dark, quick in his movements, earnest and intent in his manner.

He says, ". . . I will do a thing and then I will fear that I have done it wrong and I will recheck it. I will go through a math problem (such for instance as he has to deal with in his bookkeeping)—I know the answer—I know the figures—but I cannot feel sure that the answer is right. I know the answers are right but I cannot believe they are right. I extinguish a cigarette in an ash tray, then wonder whether it is out. The same way with a gas jet—I wonder whether it is shut off. If a flash of red, especially a neon sign, would go by, I would have that uneasy feeling and wonder if I ought not to make sure what it is."

In the extent of his anxiety and in some of his other symptoms, as well as in his personality, this patient shows himself closely akin to an anxiety hysteric; and, as an example of the phobic reaction of the anxiety hysteric, he says, "Open spaces seem to trouble me."

#### **Case VIII. Psychoneurosis with Hypochondriacal Symptoms.—**The following case is presented for the hypochondriacal symptoms which are shown. The diagnosis in

this case could be psychoneurosis, mixed type, with hypochondriasis, anxiety, and obsessional personality.

Bogart (Mr. B. N.) is a twenty-nine-year-old man with a chronically concerned expression, obese, five feet and some inches tall. He is unmarried and lives at home with his parents and siblings.

His is a conscientious personality. He works as shipping clerk for an incompetent boss toward whom he feels chronically resentful. He is somewhat defensive and competitive with his fellow workers. He plays in an orchestra without making close friends. He is justifiably but continuously worried and depressed by his parents and siblings.

Sometimes his abundant anxiety does not attach to any special idea. At other times it attaches variously to fears of suicide, of murdering his younger brother, or of causing serious physical injury to his frequently intoxicated father.

He reverts often during his treatment to feelings which he describes as "jolts in the head" and "cold drops around the heart." He is also disquieted by a theory that, as a result of his sexual abstinence associated with very rare nocturnal emissions, the semen is backing up from his testicles into his stomach. This misconception is based on an authoritatively given misstatement on physiology by an acquaintance, and he appears to give it up, at least to some extent, when he is told by his doctor that such a backing up is not possible. The jolts in the head often seem to occur in connection with thoughts of his father's hitting him on the head with a club. There is some connection between the cold drops around the heart and the attendant anxiety about death by heart disease, on the one hand, and the sudden death of a friend's mother in a church before the onset of the acute neurosis, on the other.

The *differentiation* between hypochondriasis and psychoneurosis, mixed type, with hypochondriacal symptoms is determined simply by the relative predominance of hypochondriacal symptoms over other neurotic or psychotic manifestations. One makes the diagnosis of hypochondriasis only where, as far as the case has been observed, the presenting symptoms are exclusively or very predominantly hypochondriacal in character. The bizarre character of this patient's symptoms and his misinformed pathological theorizing are typical of hypochondriasis or, in other words, are typical hypochondriacal symptoms. His moody, depressed, and aggressive personality and his murderous preoccupations are also typical concomitants of hypochondriacal manifestations. Both this patient and Mrs. W. B., the patient with conversion hysteria, were under intensive psychotherapy for five years. Mrs. W. B.



accepted treatment without payment. This patient was offered free treatment but, with almost rigid conscientiousness, insisted on paying. He finally broke off treatment, however, and disappeared, without communicating again with his physician, apparently because he resented his physician's taking a vacation. Mrs. W. B., on the other hand, clung with loving devotion to her physician and had to be practically pried out of the therapeutic situation. The contrast between the sullen hypochondriacal patient and the affectionate hysterical patient is typical.

**Case IX. Character Neurosis.**—Mr. H. H.'s wife came first under treatment with us for a nervous breakdown of almost psychotic severity. Temperamental incompatibility of husband and wife had contributed to this breakdown. Mrs. H. indicates the nature of this incompatibility by saying: "Mr. H. has a very fine character and fine men friends, but I can never get through the blank wall he presents. He is the type who, when they have brought home their entire pay envelope, feel that that is all that is necessary."

Mr. H., when he himself comes in to see us, is very neatly dressed—dark grays the predominant color, with some black. He is a man in his late thirties, dark-haired, slender, about five feet seven inches tall. He seems depressed. He criticizes himself a good deal and seems lacking in self-assurance as far as the question of human relations is concerned. Some or much of his self-criticism can be paraphrased as self-condemnation for not being emotionally demonstrative. In marriage he desires a situation in which there is emotional reciprocity rather than one in which he must be aggressively demonstrative. Though apparently wanting in assurance in respect to his human relations, he shows genuine confidence in his professional ability. His interest is rather in research than in the more remunerative executive positions in his field.

Always cooperative, he writes an autobiography at our request. In one place he writes: "In my 'teens, because of a certain shyness and lack of social poise, I felt inadequate socially and ran away from any sort of party or any organized fun-making. Very definitely I was forming what now seems to me to be a foolish pride in being uncooperative."

He saw one of us for a series of interviews. During these, the impression was formed that "he has more than normally strong feelings of social insecurity and he makes up for these feelings by verbally wounding people in a not very nice way."

Though his final decision is against further psychiatric treatment, he re-

mains on friendly terms with us and one day, in the course of an informal visit to the office, tells a story which well exemplifies the general observations of the preceding paragraph and which is incorporated in the following note made on this visit: "As to the social aspects of his professional adjustment, Mr. H. showed himself still rather bewildered and self-critical and gave the following account of his present major professional difficulty: He was in search of an assistant in his scientific work, and a Mr. Digger was recommended for the position. Mrs. H. said that he would be sorry if he accepted Digger and he himself knew that Digger was not suited to the job but accepted him just the same, doing so apparently from the wish "to be a good fellow," easy-going and cooperative, with certain of his colleagues who wanted him to give Digger the position. Digger is an older man, a good deal Mr. H.'s senior; but in the acceptance interview Mr. H. reminded Digger that he, Digger, was just a beginner and would be treated as if he were just eighteen years old. Things have worked out quite as might be expected: Digger is really no good at his job, is stupid and careless, won't tolerate criticism, and is on good terms with all sorts of people who are more political than scientific-minded. Mr. H. in his narrative displayed not the least glimmering of appreciation of his own woeful want of tact in his acceptance interview with Digger, when he had told the latter that he would be treated as if he were eighteen years old."

Let us define a psychopathologic *symptom* as a reaction which is relatively inaccessible to the individual's voluntary control and which is condemned by him as undesirable and alien to what he feels to be his real self. As the nearest approach to reactions of this sort, our interviews elicited only the shyness, noted above, and a feeling that there is "something fearsome and bewildering about large and complicated machinery." Let us define a *character trait* as a reaction usually quite automatic but relatively accessible to the individual's voluntary control and accepted by him as part of what he feels to be that real self which he defends or condemns with whatever for him is his characteristic degree of self-approval or self-censure. It will be seen that Mr. H.'s trouble-making reactions, notably his lack of skill in human relations, belong predominantly in the category of character traits and so may constitute a *character neurosis*, albeit a mild one.

**Case X. Psychopathic Personality.**—The patient's older brother came in to ask if we could help him deal with the patient, Sam.

Sam (Mr. S. C. T.) is thirty-four—two years younger than his brother. They belong to a New England family whose members have, for two hundred years, included responsible figures in the country town where they have always lived. The patient is second of six siblings. He alone stays at home with their mother and is therefore the center of her attention. He has lately mispent his portion of a recent legacy in an unsuccessful attempt to run a night club. After one automobile accident had lost him his license, he surreptitiously borrowed his mother's car and, without a license, met with another accident. The older brother bailed him out. Sam disappears from home; probably drinks during his absences. Sometimes he drinks too much at home. An older man, a bachelor, with whom Sam once lived and was in business, died and left him some money which he spent. Sam is not married: a rumor of something homosexual has come to his older brother.

Since Sam would not be expected to visit the doctor, the doctor is invited to a family luncheon in the country where he can meet Sam. Sam appears in becoming tweeds. He is rosy, blond, courteous, quiet, affable. He looks twenty-four, not thirty-four. He talks intelligently of farming and the arts. He displays a nice taste in culinary products.

Under the guidance of the older brother, the family finally resort to making Sam a remittance man. He leaves for the West to attempt ostrich farming in California. The enterprise blows up. A friend writes from California: "Last Monday Sam was over to our house for Christmas dinner and later my brother took him around to some of his friends who were having open houses. He got drunk, contacted some of my brother's friends, and made life most miserable for them. They demanded an immediate apology from my brother and are still angry with him for bringing what they termed 'an uninvited case of dementia praecox into our house and our lives.' Several days later, when his funds were exhausted, he became his usual self, which is a likeable, well-bred person of good environment." Sam departs for Mexico City in a Lincoln-Zephyr paid for no one knows how.

His brother writes: "Dear Doctor. . . Here is a letter from Sam announcing his move to Mexico City. . . ." The doctor writes back: "Dear Mr. T. . . . In reading Sam's letter . . . we are probably both equally struck by the complete absence of guilt or apology in connection with the recent fiasco and the distress which it has caused you and the rest of the family."

The diagnosis of psychopathic personality has been called the "wastebasket" of psychiatry. In cases so diagnosed we see commonly a complex of symptoms in which failure-patterns, alcoholism and homosexual trends are prominent in various combinations. But we may now claim that it is less of a wastebasket than formerly, for this diagnosis has been given more solidarity by emphasis on the defect in conscience-reactions exhibited constantly by patients with psychopathic personality, as in the case described above.

## SUMMARY

In this article an attempt is made to describe the steps in the differential diagnosis between neurosis and psychosis and then to exemplify as many as possible of the major neurotic and psychotic syndromes. In brief, the difference between neurosis and psychosis is quantitative—a matter of degree of mental disturbance. The boundary between neurosis and psychosis is not clear but roughly separates certain descriptive syndromes widely agreed upon by psychiatrists. No effort is made in the limited scope of this article to deal with the subject of treatment.

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## CLINIC OF DR. JOHN ROMANO

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### DIAGNOSTIC ERRORS IN THE NEUROSES

THE fable of the six blind men from Indostan could find no more apt application than in the multiple and divergent etiologic concepts of the neuroses. These blind men, in limiting their examination to single parts of an elephant, arrived at six different conclusions as to the nature of the beast. Similarly, the various single approaches to the study of the neurotic personality are limited in method and scope. The lesson obtained from the fable is applicable: "Each was partly in the right, And all were in the wrong!"

At the present time there is no well-defined etiologic concept or all-inclusive definition of the neuroses which will satisfy all schools of thought. However, the contributions of psychoanalysis have been of significant value in the understanding of the interplay between the endowment or potentiality of the person and his development and experience.

For clinical purposes a *classification* of the neuroses has been adopted. This, with certain variations, has included the *hysterical*, the *anxious* and the *compulsive personality*. Experience teaches us that neurotic personalities rarely exist in "pure culture," and that most of these patients have an admixture of many symptoms. Anxiety is probably the most common denominator of all neurotic syndromes. Although Freud based a classification on dynamic psychologic premises, the method of classification in most clinics is based upon description of symptoms, with little or no attempt to discover the causal psychologic mechanism.

It is not strange that the physician should be perplexed as he faces the diagnostic problem of the neuroses. There is no royal road of method, no system of mnemonics, no encapsulated group of data to which he can refer for substantiation.

The diagnosis of the neuroses is dependent upon differentiation from *organic disease*, from the *borderline psychoses* and from *conscious simulation* or *malingering*. Moreover, it is dependent upon the establishment of positive data in regard to the personality structure of the patient, to the relationship of symptoms to conflict arising from social or personal stress, to the discovery of a purpose or goal derived from the symptom, and to an understanding, if possible, of the "choice" of symptom.

It is the purpose of this clinic to point out the errors which may occur in diagnosis by exclusion alone. The physician is apt to diagnose a neurosis by exclusion of demonstrable structural disease and the major psychoses. This step is necessary. The error lies in the inference which follows negative data, *i. e.*, that as there is present neither somatic disease nor major psychosis, the patient's symptoms must necessarily be considered as of neurotic origin. This does not imply that each neurotic patient should not receive thorough and painstaking physical, neurologic and indicated laboratory examinations. Nor does it imply that neurotic patients should not be re-examined at intervals. The error lies in the fact that the absence of physical findings or of flagrant psychotic symptoms, in itself, does not constitute evidence for neurosis. It is necessary to obtain further data in order to disclose the neurotic structure of the personality and the specific neurotic value of the symptoms.

#### ILLUSTRATIVE CASES

The histories of two patients will be presented to illustrate the point that *structural disease* must be excluded in the diagnosis. Preliminary study of both patients revealed no demonstrable physical abnormality and neither was psychotic. Because of these negative findings, they were called neurotic.

In neither was it possible to demonstrate any pertinent neurotic structure. In the first patient this led to further search for cause; in the second patient, more complete description of his attacks led to the correct diagnosis.

**Case I.**—A twenty-two-year-old machinist entered the hospital complaining of pain in the back and epigastrium occurring every night for the preceding six weeks. About two months before entry the patient had had an episode of epigastric pain which lasted four to five hours, was said to be due to an "ulcer" by his local physician, and was unsuccessfully treated with diet and powders. Six weeks before admission the patient noted the onset of severe, boring, bilateral pain in the lower thoracic region of his back, coming nightly at about 1 A. M. It was not related to sleep or to activity and it was not relieved by food. Because of the persistence of this symptom he entered the hospital where physical examination revealed slight diffuse epigastric tenderness.

All laboratory findings were within normal limits. Roentgen examination of the gastro-intestinal tract, gallbladder and spine were essentially negative, and following an attempt at dietary therapy the diagnosis of neurosis was entertained. However, psychiatric examination failed to elicit neurotic personality traits or show a chronologic relationship of the symptoms to stress situations, nor was there a purposeful gain derived from the symptom. Accordingly, further roentgen studies were made and these revealed a destructive lesion in the eighth thoracic vertebra, suggestive of a tuberculous process.

**Case II.**—A forty-four-year-old medical technician was admitted to the hospital because of recurrent episodes of confusion. Past history revealed that he had experienced these episodes over a period of five years. On previous hospital and out-patient admissions he had been studied intensively but no significant findings were noted.

Circumstances, including the patient's war experiences and the nature of his work (preparing cadavers), led to the diagnosis of an hysterical fugue state. With some study, it was found that the patient resented the domination of a senior fellow employee and it was believed that this unexpressed resentment was a pertinent factor in the precipitation of his attacks. However, after the patient was liberated from this stress, he continued to experience these episodes of confusion and motor restlessness.

It was possible at this time to obtain more complete data as to the specific nature of the episodes. Eventually the diagnosis of a hypoglycemic state was made, which was confirmed by further study. More detailed studies of the patient in a normal state, as well as in experimental insulin shock, failed to reveal causal or coincidental psychogenic factors. Surgical exploration revealed an islet-cell adenoma of the pancreas which was removed. There has been no recurrence of symptoms, nor has it been possible to demonstrate any pertinent neurotic symptomatology.



A second source of error lies in the attempt to exclude *psychotic reactions*. In most instances, this exclusion is based upon a limited understanding of the signs and symptoms of the psychoses. There is considerable difference between the caricatured textbook description of a depressive psychosis and the borderline or early stage of some depressive reactions. Many schizophrenic psychoses are prefaced by anxious, obsessive or hypochondriacal symptoms, long before the patient expresses bizarre conduct or delusional trends. It is necessary to differentiate the psychotic state from the neurotic. It cannot be done until there is fuller appreciation of the borderline psychoses. Actually, the exclusion of psychotic state in the traditional sense does not always rule out psychosis, nor does the exclusion, per se, constitute absolute evidence of neurosis.

In the following case, the diagnosis of an hypochondriacal neurotic condition was entertained because the symptoms were not explained by the physical findings and because the condition of the patient did not correspond with any advanced psychotic state.

Case III.—A fifty-four-year-old unemployed bartender was admitted to the hospital with the presenting complaint of pain in the lower left quadrant which radiated to the groin. In addition, he complained of headache and tight feelings in the top of his head, and expressed concern over the function of most of his organs. Physical examination revealed some tenderness in the lower left quadrant and along the course of the inguinal canal. He was found to have a left inguinal hernia. His multiple complaints were interpreted as due to a hypochondriacal neurotic reaction. Further history revealed the fact that he had experienced a depression at the age of twenty-one, following divorce from his first wife. The onset of his present symptomatology dated to 1929, following economic reverses. At that time he was depressed in mood, and somewhat retarded in activity and in initiative. Since then he has had intermittent periods of depression with exacerbation of his symptoms.

Mental examination showed the patient to be retarded, concerned with feelings of inadequacy and forlornness, and with considerable hypochondriasis. His appetite was fair but he had lost 10 pounds. He experienced early morning awakening with diurnal swings of mood. He was constipated and felt slowed and tired all over. He had some feelings of unreality. The condition was interpreted to be a depression, possibly reactive to certain social and personal stresses. After herniorrhaphy had been performed he was advised to return to the psychiatric clinic.

The following report presents the opposite situation. Organic disease was suspected as the cause of this patient's disability; however, physical examination, together with laboratory tests, revealed no significant findings. After study of the personality structure, the situation which the patient faced and the specific symptoms, it was possible to establish a diagnosis of a neurotic personality with anxiety and conversion symptoms.

Case IV.—A fourteen-year-old school girl was admitted to the hospital because of aching of the back and legs for four weeks. Physical, neurologic and laboratory observations were within normal limits. During infancy and childhood the patient had become remarkably aware of her physical condition. This had been conditioned by a series of injuries and physical diseases which she had experienced, by the description of symptoms and signs by parents, relatives and friends similarly affected, and by the solicitude and concern of a mother who was partially disabled from anterior poliomyelitis. In early life the patient had manifested certain symptoms which were productive of attention and care. New and more mature adjustments were often partially solved by symptom formation. These usually took the form of weakness or of diffuse aches in the regions of the body previously injured. A similar condition seemed to exist at this time. Recently the patient had been promoted to high school where she found the new teachers, strange companions and a quickened tempo of activity to be a considerable source of tension. She had been concerned with her mother's health and with the embarrassed financial status of the family. In addition, she had suffered from a mild afebrile upper respiratory infection which had prostrated her in a manner not accounted for by the objective signs. This prostration and weakness had persisted for four weeks.

During the interviews the patient recounted her story spontaneously and with little hesitation. On a number of occasions, while describing her school activities, she became tense, picked at the bedclothes and was observed to have an increased pulse rate. She was very alert and her intelligence was estimated to be within normal limits. The patient was considered to be an anxious, sensitive child of average intelligence who attempted to solve a difficult situation by symptom formation. A precipitating factor may have been the respiratory infection with its usual sequel of fatigue. Presented with a situation which demanded change and a more mature adjustment, it is possible that the patient utilized the symptoms to which she had been conditioned. In this way it was possible for her to solve the dilemma by escape into illness.

The *therapeutic program* in this case consisted of four avenues of approach. First, in a simple and repetitive manner it was explained to the patient that she had no demonstrable organic disease and that there was no reason to be concerned

with "neuritis," "arthritis," "infection," and so forth. Second, by simple analogies the rôle of certain obvious emotions, such as fear and anger, in producing or modifying physiologic function was explained to her. Third, the specific factors in her background which had led to certain symptoms formation and the current stresses which had precipitated the symptoms were discussed in detail. Last, an attempt was made to alter the immediate environment. Interviews were held with the mother so that she and the father would be able to understand the significance of the symptoms and to deal with them more effectively. A tutor was assigned to the patient so that she could resume gradually her school work without undue stress. The reassurance and encouragement of the ward nurses aided in her immediate rehabilitation. The patient was discharged to her home after a period of a few days. Five months later she is stated to be symptom-free and to be making a satisfactory adjustment in school and at home.

#### COMMENT

**Importance of the Neuroses in General Practice.**—A certain proportion of patients examined by the general practitioner exhibits neurotic personalities complicated or uncomplicated by physical disease. It follows logically that the physician should be prepared to identify, understand, and treat the neuroses of these patients. Obviously, the complexity of certain problems necessitates highly skilled technics, but there remains a great number of patients who can be understood and helped without recourse to them. More than the requirement for special technical skill, there is a need for an attitude of awareness of the psychological factors in illness. Owing to the great advances of knowledge in the basic medical sciences, there has been an uneven emphasis on cellular and organ physiology as contrasted with the totality of the organism. This has led to an accentuation of the mind-body dichotomy so that the student and the physician find it difficult to understand or accept the significance of psychogenic phenomena

in qualifying, precipitating or causing illness. Emotional and somatic aspects of illness co-exist and are interrelated.

Errors in diagnosis of the neuroses are frequently due to the acceptance of negative data alone. In addition to the exclusion of organic disease and the major psychoses, it is necessary to discover certain data which are more or less specific to the neurotic personality and its manifestations. In some patients this is extremely difficult and entails considerable study. In others, it may reveal itself more readily.

**Method of Examining the Neurotic Patient.**—Obviously, this search for more positive data is dependent upon a method, and it is a method that differs from the traditional psychiatric examination. The latter was originally intended for the study of the psychotic person, and its use with neurotic patients or with patients who are physically ill and in whom one suspects neurotic symptoms is inadequate and, at times, quite provoking. It is necessary to incorporate into the usual medical history and physical examination an attitude of awareness of psychological factors and a means of evaluation of personality.

The patient should be allowed to tell his story spontaneously and without interruption. The physician should note the *organization of the content*, the exaggeration, casualness or distortion of certain topics, and the forgotten incidents. Some of these data may be obtained in one interview; others will be gained in repeated interviews. The form or *manner of presentation* is as important as the content of the story of illness. Objectively, there may be evidences of tension, motor restlessness, tremor, sweating or blushing while the patient is recounting certain data of emotional significance. More specifically, determination of the *emotional state* of the patient before, during and after the onset of the present illness may contribute significant information. The time of day, place of occurrence, and the resemblance of the patient's symptoms to those he has experienced previously or to those of a friend or relative may be of value. In the latter one may detect the presence of

*psychological identification* which may be a pertinent factor in the "choice" of the symptom.

It is important to evaluate the *personality structure* of the patient. This may be done in a variety of ways but, for practical clinical purposes, will necessarily include an interpretation of the patient's performance in the past and present. In many instances the necessary information will have been obtained during the spontaneous recitation of the history. At other times it will be necessary to obtain further information from the patient or from other sources. It should include an interpretation of the patient's attitudes to and the influences of his siblings, parents, mate and children; his sexual adjustment and energy output; the character and intensity of his prevailing moods; the presence of anxiety or tension in periods of stress; his reactions to failures and successes; his acceptance or rejection of reality; his intellectual development and work performance; his attitude to friends, fellow workers and group interests; his attitude toward his body, to health and disease, and to the specific illness. If one is able to obtain some or all of the above data he will be aided in interpreting the significance of the symptoms in the setting of the individual personality.

In addition to this, some type of *mental status examination* should be made. It is better to utilize an indirect and informal method of inquiry than to follow slavishly a question and answer technic. Here again, it will not be necessary to repeat certain examinations. The patient's attitude and general behavior have been manifested throughout the examination. The form and content of his speech have been exemplified. The spontaneous recitation of his history will have given many leads as to the mood and the form and content of thought. Sense deceptions may have objective manifestations. The sensorium need not be tested in a rigidly pedantic manner if the patient has presented a logical sequence of events, if his intellectual endowment appears to be within normal limits, and if there is no evidence of defect in awareness.

These suggestions may be utilized to interpret the personality structure of the patient, to reveal the chronological relationship between the symptoms and personal or social stress situations, to demonstrate the purpose or gain derived from some neurotic symptoms, and to explain the "choice" of certain symptoms. In addition, it is suggested that one should adopt some type of mental status examination in order to identify the borderline psychoses.

#### SUMMARY

The diagnosis of the neuroses is dependent upon the differentiation from organic disease, from borderline psychoses, and from malingering. Moreover, it is dependent upon the establishment of positive data in respect to the neurotic personality and to the neurotic character of the symptoms.

Errors in diagnosis frequently occur when they are made by exclusion. The absence of physical disease is not absolute evidence of neurosis. The absence of the major psychoses does not always exclude the possibility of a borderline psychosis, nor does the exclusion, *per se*, constitute evidence for neurosis.

Suggestions are offered for a method of study of personality and of evaluation of symptomatology.



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### DIFFERENTIAL DIAGNOSIS OF COMMON INFECTIOUS DISEASES

SORE throat and skin rashes are among the most common conditions for which the family physician is consulted in the field of the common infectious diseases. I propose, therefore, to discuss these two major symptoms from the standpoint of differential diagnosis, along with a few brief remarks on treatment, and in addition to say a few words about whooping cough and mumps.

TABLE 1

ETIOLOGIC AGENT, INCUBATION PERIOD AND DURATION OF INFECTIOUSNESS OF THE COMMON INFECTIOUS DISEASES\*

Disease.	Etiologic agent.	Average incubation period, days.	Usual duration of infectiousness.
Common cold.....	Virus	1	During acute phase.
Tonsillitis.....	Bacteria	1	During acute phase.
Diphtheria....	Bacteria	3	Duration of positive cultures.
Chickenpox...	Virus	15	Until free of scabs.
Smallpox...	Virus	12	Until free of scabs.
Measles.....	Virus	12	Three days before and five days after duration of rash.
German measles...	Virus	15	Duration of eruption, four days.
Scarlet fever.....	Bacteria	3	Three weeks, unless complications are present.
Whooping cough..	Bacteria	9	Three to six weeks according to severity.
Mumps.....	Virus	18	Two days before and four days after the height of the swelling.

\* All of these are variable. Some patients with diphtheria and scarlet fever, even though showing negative cultures, on discharge from isolation promptly infect others. In the virus diseases and whooping cough, the infectivity usually precedes the date of diagnosis and decreases from then on.



## SORE THROAT

The term "sore throat" is a rather ambiguous term as it includes all those disagreeable sensations which may arise anywhere from the postnasal space to and including the larynx. The common cold, in its origin a virus disease with fluent coryza, may begin with a sore throat in which the congested follicles on the posterior pharyngeal wall present the only visible pathology. Since these are often congested during the winter months, the important feature remains that the patient complains of the throat being sore. The inflammation may be confined to the nasopharynx, giving rise to a burning sensation in this area which sometimes precedes the coryza. However, this virus may activate other pathogenic organisms, which can bring about a much more severe inflammation and one of a protracted character. Influenza may also start as a sore throat, but like the virus of the common cold it is capable of activating other organisms in this region, notably the streptococcus. Many other infections of virus origin, such as measles, German measles, mumps, and poliomyelitis may begin with the complaint of a sore throat in which congested lymphoid tissue is apparent. Indeed, the complaint may have its origin in enlarged lymphatic glands which cause pain on swallowing.

**Tonsillitis.**—Tonsillitis is usually of streptococcal origin, but it can also result from a wide variety of pathogenic organisms. Assuming the tonsils to be in the nature of a first line of defense, it is natural that they should become invaded in the course of many different infections. In the course of repeated invasions they may become a liability as ineffectual barriers and harbor pathogens. Until there is evidence that the tonsils have become a liability, *they should not be removed*. Statistical studies on the relation of tonsillectomy to subsequent susceptibility to the common infectious diseases and their complications have engendered a conservative attitude with respect to this operation.<sup>1, 2</sup> In scarlet fever, for instance, it has been shown that the incidence of otitis media,

mastoiditis, sinusitis, and nephritis is not reduced through a previous tonsillectomy.<sup>3</sup>

The common variety of tonsillitis presents a picture of swollen and inflamed tonsils, with points of yellow or white exudate in the crypts. These points of exudate enlarge and eventually coalesce over the surface of the tonsil, but this exudate tends to remain confined to the surface of the tonsil. If removed it is easily crushed like soft cheese between two tongue depressors.

**Beta-hemolytic Streptococcal Infections.**—In certain beta-hemolytic streptococcal infections, such as *epidemic sore throat* and *scarlet fever*, there may be patches of thin white membrane on the tonsils as well as on the uvula or soft palate. These are true fibrin deposits and bleed when removed. The important feature is that they remain thin. The fauces are red and angry, and there is often edema of the uvula, soft palate, and even in the neck. There is usually high fever, backache, and pronounced malaise. In these cases throat cultures should be taken for the Klebs-Loeffler bacillus. The use of *sulfanilamide* in ordinary tonsillitis of streptococcal origin has not been proved to be efficacious in reducing the fever, ameliorating the symptoms, or avoiding complications.<sup>4</sup> Nevertheless, when the streptococcus invades the deeper tissues, and especially in the event of a bacteremia, vigorous chemotherapy is indicated.

**Peritonsillar Abscess.**—Peritonsillar abscess frequently supervenes on a bilateral tonsillitis, forcing the surfaces of the tonsils into close proximation out of the midline. The uvula in these cases is often edematous and distorted. The soft palate bulges over the abscessed side. In skillful hands an incision can be safely made to evacuate the pus, but many of these open spontaneously.

**Retropharyngeal Abscess.**—A retropharyngeal abscess, particularly if low, can give rise to difficulties in diagnosis. There is pain on swallowing and obstruction to breathing if the neck is flexed or extended. Opening the mouth wide, or

downward pressure on the tongue by the examiner, also tends to shut off the air passage.

*Case 1.—Retropharyngeal Abscess Mistaken for Bulbar Poliomyelitis.*—A nine-year-old boy was sent to the hospital as a case of suspected bulbar poliomyelitis at a time when this disease was epidemic. He complained of inability to swallow and difficult breathing at times. Respiration was regular and quiet unless he tried to swallow, when he would choke. There was no crowing respiration as in laryngeal obstruction. There was no evidence of paralysis of the diaphragm or intercostal muscles. There was marked rigidity of the neck and spine. Examination of the fauces was very unsatisfactory as the boy would not open his mouth wide and resisted attempts to use a tongue depressor. A quick digital examination of the fauces revealed a bulging mass on the posterior pharyngeal wall. The white blood count was 18,000 with 84 per cent neutrophils. Dr. Edwin H. Place incised the abscess, after which there was immediate relief from all the symptoms.

**Faucial Diphtheria.**—Faucial diphtheria in its mildest form may give rise to only a slight sore throat, with or without a patch of white membrane, and only a slight fever. These cases are easily missed unless a *culture* is taken. Without membrane formation there is difficulty in the diagnosis even with a positive culture, because the patient may be a diphtheria carrier and be coming down with a mild tonsillitis in which the diphtheria organisms may play a secondary part. However, the discovery of such a carrier always serves as valuable information regarding his care, as he is to be treated for diphtheria. Some cases of diphtheria show only a small thin white membrane. The *Manzulla test* consists of applying with a cotton swab a 2 per cent aqueous solution of potassium tellurite to the suspected throat lesion. In the presence of diphtheria the lesion turns black. This test is not infallible,<sup>5</sup> but neither is a single negative culture.<sup>6</sup>

In the more *severe* form, the patches of membrane thicken as they spread like lava beyond the confines of the tonsils, over the pillars, onto the uvula, soft palate, and over the posterior pharyngeal wall, becoming a dirty gray, a dark green, and finally black in places. If a piece is pulled off a bleeding surface is left. If placed between two tongue depressors it is like wet leather and cannot be crushed. There is a charac-

teristic foul, fetid odor which fills the room. At this stage the membrane often rests on a swollen, convex surface with a bluish tinge to the surrounding tissue. This edema may extend to the neck and give rise to the so-called "bull neck." These advanced cases are unmistakable. The fever is usually not as high as in the streptococcus throats of equal severity. The toxemia in advanced faucial diphtheria, particularly in children, is apt to induce a state of listlessness and apathy.

*Restlessness* in faucial diphtheria should always be regarded with suspicion because it is apt to denote respiratory obstruction. For this reason opiates are to be avoided in the membranous stage, as they mask the indications for intubation and tracheotomy. The same holds true in severe streptococcus cases. Antitoxin is essentially protective, and to be effective must be administered early. In neglected cases it is a common experience to see a marked temporary improvement from antitoxin, only to have the patient succumb from a myocarditis or vascular collapse. Dehydration often results from difficulty in swallowing. Furthermore, the toxin disturbs the carbohydrate metabolism. Therefore, 10 per cent dextrose given intravenously is indicated, and in severe cases this is often continued daily until the patient is able to take adequate nourishment. The use of vitamins C and B<sub>1</sub>, even in large doses, has not yielded the encouraging results we had hoped for. The cardiovascular and neurologic disturbances do not come under the scope of this discussion.

**Ulcerative Sore Throat.**—Three types of ulcerative sore throat must be mentioned: the *syphilitic*, which is relatively less painful than other kinds; *Vincent's angina*; and *agranulocytic angina* (granulocytopenia), the last two being more often associated with an ulcerative stomatitis. Diagnosis is established in the first of these by the Wassermann reaction, in the second by stained smears for the spirillum and fusiform bacillus, and in the third by the white blood count and differential count. The finding of a marked leukopenia should prompt one to inquire whether amidopyrine or related drugs have been taken. In Vincent's angina it is well to have the blood sugar

estimated, since diabetics are prone to show these saprophytic organisms. The local treatment in our wards consists of sodium perborate as a mouth wash and gargle. It may also be used as a paste. In obstinate cases arsphenamine powder is applied directly to the lesion with a cotton swab. In agranulocytic angina we have used pentnucleotide intramuscularly with varying yet encouraging results.

**Laryngitis.**—Laryngitis may well be considered under the heading of sore throat. Simple croup is probably often of virus origin, but the severe forms are due largely to the diphtheria bacillus and the streptococcus. The smaller the larynx, the more quickly do the signs of suffocation come on, with crowing respiration and recessions of the sternum on each inspiration. Some of these patients hold their color well in spite of labored respiratory efforts, and recover under pure steam vapor, which is preferable to admixtures of the compound tincture of benzoin, eucalyptus, and anise.

Fatigue and cyanosis call for *intubation*. In the case of diphtheria under antitoxin treatment, the tube can be left in for several days, and sometimes it is coughed out as the swelling and membrane disappear. But in the streptococcal form, ulceration tends to take place about the tube. Consequently it is left in only long enough to give the patient a rest from his violent respiratory efforts, and to serve as an airway during the tracheotomy, at the completion of which extubation is done. Direct laryngoscopy is often *desirable*, but this process may induce a spasm which necessitates immediate direct intubation.

*Case II.—Croup of Unknown Origin—Possibly Virus.*—A baby, eighteen months old, was admitted for croup with restlessness and recession of the sternum with each inspiration. The color was normal. The patient had been immunized against diphtheria six months previously. Examination of the fauces was essentially negative, but this examination precipitated a violent coughing fit with an increase in the recessions. Steam vapor was run into a tent covering of the crib, after which the patient slept in short naps. The next day the patient's breathing was normal, and three days later he was discharged. No medication of any kind was used. Cultures from nose and fauces taken on admission proved negative for diphtheria.

*Case III.—Streptococcal Laryngitis.*—A baby of nine months was admitted at 6 A. M. for croup with marked recession of the sternum, cyanosis, and bulging of the eyes. The fauces were only slightly congested. Laryngoscopic examination showed a bright red larynx with edema and without membrane. Direct intubation was done, and 5000 units of diphtheria antitoxin were given on general principles, after which the child promptly fell asleep. Cultures from the nose, throat, and larynx were all negative for diphtheria and positive for hemolytic streptococci. The next day tracheotomy was performed under local anesthesia. Sodium perborate solution was dropped into the tracheotomy tube to loosen crusts, which were coughed out. The inner tracheotomy tube was closed with a stopper on the seventh day and removed on the ninth day, the wound being closed with an adhesive strip. The voice returned to normal.

The use of *sulfanilamide* in these cases of streptococcal laryngitis *has not been at all encouraging*. In fact, this drug has the disadvantage of inducing a cyanosis which might be mistaken for anoxemia, precipitating operative interference which might be avoided. Tracheotomy is always attended by the risk of bronchopneumonia, and the preliminary step of intubation should never be done unless the situation becomes critical. Some of us now prefer to avoid the use of sulfanilamide for fear of hampering our judgment regarding the necessity of a tracheotomy. *Sulfathiazole*, which does not induce cyanosis, is now being used in these cases.

## RASHES

The difficulties which arise in the diagnosis of rashes of infectious origin lie in the modifications of their severity. As an example, severe chickenpox may be confused with smallpox, and mild smallpox may be mistaken for chickenpox. One must keep in mind the salient diagnostic features of these two diseases, some of which will almost always be sufficiently in evidence to enable one to differentiate the two diseases under these circumstances:

**Chickenpox.**—In chickenpox the prodromal period is often absent or it is relatively mild in character. The vesicle may be preceded by a brief pink papule, and then become superimposed on the papule which forms a corona; or vesicles may arise with the merest vestige of a pink base. These are

unilocular, and come out in crops. In as short a period as eight hours a vesicle may start to dry up, but usually the scab takes longer than this to form. However, at the end of twenty-four hours there will usually be lesions in all stages of development. In the severe eruptions the lesions are apt to be most numerous on the body. When in doubt, one generally looks for a *vaccination scar* in the way of circumstantial evidence against smallpox.

**Smallpox.**—In smallpox the prodromal period is in proportion to the eruption which is to follow. Often the chill, intense backache, and high fever are mistaken for the onset of influenza, and this may go on for three days with a short temporary improvement just before the eruption appears. The prodromal rash is often morbilliform with petechiae, and this may last for twenty-four hours before the vesicles form. These tend to come out all at once in one crop, except that those on the face may precede those elsewhere on the body. Nevertheless, all those on the face will be in about the same stage. They also tend to coalesce and are thus multilocular. They arise from a deeper layer of the skin, and sometimes give rise to a “shotty” feeling before they emerge from the papular base. The covering of the vesicle is thicker and firmer than in chickenpox. In the severe cases the lesions are most numerous on the face, forearms, and legs.

After a few days the vesicles become pustules, and their surfaces become indented. In the course of a week scabs begin to form irregularly, and the fever gradually subsides. In mild smallpox the few scattered lesions have these same characteristics, especially their simultaneous appearance, protracted development, and relative depth. There are many other features of importance in this disease, but these salient features form a basis of diagnosis. The *early* stage must be differentiated from *influenza*, *measles*, *typhus*, and *syphilis*; the *later* stage from *impetigo contagiosa*, *pemphigus*, and *straw itch*.

**Measles.**—Measles (*rubeola*) may present several difficulties in diagnosis through modification of the usual signs. Mild

catarrhal symptoms with slight fever may continue for three or even four days before the rash appears. The cardinal symptoms of coryza, conjunctivitis, and cough may be very slight indeed. In fact, in very mild cases these symptoms may be entirely absent in spite of careful daily examinations done because of a known exposure. This is particularly true in the modified forms after convalescent serum or placental extract has been used.<sup>7</sup> The coryza is apt to be more in the nature of a snuffle with sneezing, and only rarely a fluent coryza. The various eye signs which have been described are not usually pronounced until the day the rash appears. The cough also is likely to be held in abeyance until this time, although the constant hacking cough so characteristic of the disease may precede the eruptive phase.

*Koplik spots* are the really important prodromal signs, but even these may not appear until the first macules have broken out. On the other hand, I have seen them clearly four days before the rash with a preliminary fever, after which they disappeared and the temperature was normal for two days. Then on the fourth day, the fever rose abruptly and a severe rash blossomed forth, with conjunctivitis and a persistent hacking cough. Sometimes a few small macules appear on or about the neck and then fade away. This quiescent period reminds one somewhat of what may take place in some other virus diseases, namely, smallpox, poliomyelitis, and the eastern strain of equine myeloencephalitis. The Koplik spots resemble grains of white pepper with small bluish haloes about them. They occur on the buccal mucous membrane, sometimes also on the gums. They are best seen with daylight, but at their height they are clearly seen with a flashlight. One must be careful not to stretch the cheek with a tongue depressor as this tends to blanch the small halo of congestion, making it more difficult to recognize this early sign. They are to be distinguished from the large and pure white spots of *thrush* in infants, and from *aphthous stomatitis* with its widely scattered yellowish vesicular lesions. The conjunctivitis is in itself the important eye symptom.



The rash itself should give no difficulty in its characteristic form. The macules appear first on the neck and face, and spread rather rapidly over the trunk and extremities, becoming confluent. Fading begins in twenty-four or forty-eight hours, the macules exhibiting a pigmentation which may be in evidence for five or even ten days, according to the severity. As compared with German measles and scarlet fever, the rash has a bluish look when it is full blown. In *German measles* there may be well-marked conjunctivitis. In *erythema multiforme* and *syphilis*, the lesions are circinate, of much longer duration, and unaccompanied by the catarrhal and conjunctival symptoms. *Roseola* (exanthem subitum) is apt to be more punctate, and is preceded by several days of fever, the eruption appearing as the fever subsides, in contrast to measles where the rash and fever reach their peak in the same twenty-four hours. *Serum rashes* are urticarial in character and accompanied by itching; yet at times the eruption may resemble measles, German measles, or scarlet fever. Again the conjunctival and catarrhal symptoms are lacking. These serum rashes respond to adrenalin. Measles does not. Macular eruptions may occur from aspirin, antipyrin, acetanilid, phenobarbital, and from sulfanilamide and its allied compounds.

**German Measles.**—German measles (rubella) may begin with mild symptoms of a cold and sore throat, lasting a day or two. Small red spots are sometimes seen on the soft palate. The rash breaks out first on the face and spreads in a very few hours over the trunk. At the beginning the eruption is often macular, but these macules are smaller, discrete, and of a pinker hue than in measles. Within twenty-four hours the rash changes into a punctiform type suggestive of scarlet fever. This *kaleidoscopic character* of the eruption is of diagnostic importance: it may suggest measles at first, then scarlet fever—or even vice versa—and then be gone on the third day. In severe cases, especially in adults, there may be a well-marked conjunctivitis. This and the pronounced distribution over the face distinguishes these cases from scarlet fever. A very important feature is the *enlargement of the lymph nodes*, either

behind the ears or extending down the back of the neck from just below the occiput. The posterior auricular glands may continue to remain enlarged indefinitely. The only serious complication of this disease is encephalitis, which is very rare.

**Scarlet Fever.**—Scarlet fever is caused by a group of beta-hemolytic streptococci capable of elaborating an erythrogenic toxin. It is characterized by a period of invasion with a sore throat and fever. In children there is often vomiting. The sore throat may persist for three or four days before the rash. Only those individuals who are susceptible to the toxin react to this infection with a rash. Those not susceptible to the toxin will show only a sore throat and fever when infected. Most children are susceptible to the toxin, and therefore they develop the rash. Most adults are immune to the toxin, as shown by Dick tests and clinically by their failure to succumb to the infection when exposed.

The *sore throat* of scarlet fever is like that already described under the streptococcus sore throat with all variations of severity. However, there is added to this the element of the toxin. This is manifested in an enanthem over the soft palate characterized by a punctiform redness with minute petechiae.

The *exanthem*, or skin rash, comes out first over the upper part of the neck, chest, abdomen, and back, extending to the extremities. The face almost invariably remains clear, but there may be a hectic flush with pallor about the mouth. This circumoral pallor is seen in many other febrile conditions associated with vomiting. In severe types there may be some rash on the temples. In the early stage it is apt to be most marked on the neck and about the axillae and groins. In its mildest form it is diffuse bright red erythema. As the severity increases the punctiform character becomes manifest, and this is often superimposed on the diffuse erythematous base. In the most severe forms the skin assumes an almost livid hue. The important features may best be kept in mind through the pathology. The toxin causes a dilatation of the capillaries of the skin, hence the erythema. The capillary tufts in the

papillae become engorged, hence the punctiform element of the eruption and the gooseflesh roughness. This congestion in the capillary tufts causes miliary vesicles to form on their summits. In the Negro these vesicles become minute white spots. The congested capillaries in the folds of the skin tend to rupture; hence minute hemorrhages occur in the axillae, the groins, and on the anterior aspects of the elbows. In severe rashes this hemorrhagic tendency is seen over the trunk in the form of petechiae, and the eruption over the entire trunk takes on a coppery hue from these minute extravasations. Constriction of the upper arm by a tourniquet causes showers of petechiae to appear on the forearm, the Rumpel-Leede sign. It is an unreliable sign in mild rashes, and entirely unnecessary in pronounced scarlet fever.

If scarlet fever comes on during a *sunburn*, the sunburned portion of the skin will show an accentuated vesicular element, true blistering—in striking contrast to the areas not sunburned. On the other hand, if the skin has become tanned, the tanned areas may show little or no evidence of rash, while the untanned areas may show a marked rash, often of the vesicular type.

The *tongue* is at first coated, but the same pathology is present. The papillae become engorged. This is first seen on the tip and on the sides, but in time the papillae are seen emerging through the white coating. Eventually as the coating comes off, these papillae stand out prominently, giving rise to the “strawberry tongue.”

After a mild rash, *desquamation* may begin between the fourteenth and twenty-first day, but in severe rashes a primary desquamation begins often in the first week, especially about the neck and wherever miliary vesicles have been abundant. The later desquamation is seen most markedly on the palms and soles, often beginning about the tips of the fingers and toes.

The *complications* of scarlet fever do not concern us here, except for the reminder that they may occur with the onset of the disease, especially in those cases with a so-called septic

onset showing a purulent rhinitis or severe tonsillitis. In some instances, sinusitis, suppurative otitis media, and cervical adenitis may even precede the rash. These septic complications are due to the pyogenic properties of the streptococcus and not to the toxin. It is the latter which offers us the diagnostic criteria.<sup>8</sup>

*Surgical scarlet fever* is the term given to a wound infection with this group of streptococci in individuals susceptible to the toxin. This is differentiated from ordinary scarlet fever originating in the throat, where a surgical operation is performed during the incubation period. Burn scarlet fever is of a similar nature to surgical scarlet fever in that infection takes place in the wound.

The *blanching test* (Schultz-Charlton reaction) consists of injecting 0.2 cc. of a 1:50 dilution of the Dick antitoxin or of a pooled scarlet fever convalescent serum. If this test is made during the first forty-eight hours, the site of the injection will show a blanched area within about twelve hours. In those fleeting rashes which give the most trouble in diagnosis this test is of little or no value as the rash is often gone before the blanching begins. In those cases where the rash lacks the usual distribution and appears only in a few areas, such as is seen sometimes in puerperal scarlet fever, the test is often of great value.

In the *differential diagnosis* of scarlet fever, one must keep in mind that the scarlatiniform eruption of German measles involves the face. The same holds true of the erythema which occasionally accompanies influenza. The rare prodromal eruption of chickenpox can be confused with a mild fleeting scarlet fever rash. Serum rashes simulating scarlet fever are apt to involve the face, but they invariably present the elements of urticaria.

**DRUG ERUPTIONS.**—Drug eruptions deserve special consideration. In the first place, they involve the face. This is particularly true of that rare skin reaction to quinine which, except for this facial involvement, may closely simulate the scarlet fever rash, even to the desquamation.

*Case IV.—Drug Eruption (Quinine).—*A twenty-eight-year-old school teacher developed tonsillitis for which he was given a combination pill. Thereupon he developed a pronounced scarlatiniform eruption which was well-marked on the face. The patient was sent to Haynes Memorial Hospital with the diagnosis of scarlet fever, but he was put in special isolation because of the pronounced rash all over his face and because he protested that the rash was similar to that experienced by him twice before after quinine administration. The papillae on the tongue were slightly prominent but not red. The blanching test was negative to both Dick antitoxin and pooled convalescent serum. There had been no known exposure to scarlet fever. On inquiry it was learned that the pill had contained quinine. The rash lasted five days and was followed by marked desquamation throughout, especially of the palms and soles. Throat culture showed streptococci, but these were not toxin producers. The tongue showed no change. The diagnosis here was erythema medicamentosa (quinine) and tonsillitis.

*Belladonna* may produce an erythema, but with it there is a dryness of the throat rather than inflammation of the fauces. *Aspirin* can produce a scarlatiniform rash, but it is blotchy. I saw one such case with an angioneurotic edema of the uvula and soft palate. The internal and external use of *mercury* can give rise to a brilliant diffuse erythema:

*Case V.—Drug Eruption (Mercury).—*A girl of seven who had been treated for extensive impetigo contagiosa with ammoniated mercury ointment for one week was sent to the hospital with a diagnosis of scarlet fever. The temperature was 100° F. and the fauces were slightly injected. There was no salivation or stomatitis. A blotchy scarlatiniform eruption on the trunk and extremities had been present for forty-eight hours. The tongue was entirely negative. A diagnosis of mercurial poisoning was made on admission and confirmed by negative blanching tests. The rash lasted twelve days. Desquamation was confined to the areas of the eruption.

The *arsphenamine* rash is an intense diffuse erythema involving the face and characterized by a branny desquamation which begins soon after the height of the eruption. All forms of dermatitis exfoliativa are protracted beyond the eruptive period of scarlet fever.

TREATMENT OF SCARLET FEVER.—The treatment consists of the usual care given in the case of a fever. After the febrile stage is passed the diet should be that in accordance with the age of the patient. An impoverished diet may favor the development of complications. Severe cases often show

dramatic results from the Dick antitoxin or convalescent serum if administered within forty-eight hours. Sulfanilamide has no effect on the rash or the fever; but if a maintenance dose is kept up the complications appear to be diminished. This, however, is achieved only at the risk of added days of illness from the drug itself.<sup>9</sup>

### MISCELLANEOUS INFECTIONS

**Whooping Cough.**—Whooping cough may start as a common cold, with sneezing, lacrimation, and a dry cough. In babies the sneezing may be of a pronounced paroxysmal character and persist throughout the attack. Often the first symptom noted is a persistent cough of a dry or a loose character. After about a week the cough becomes paroxysmal and staccato, interspersed with deep inspirations which constitute the whoop. During the paroxysm the tongue may protrude and a stringy mucus drip from the mouth.

One should keep in mind that a foreign body in the fauces or lower air passages can give rise to a paroxysmal cough, sometimes even with a whoop.

*Case VI.—Paroxysmal Cough with Whoop Caused by a Foreign Body.*—A baby suddenly developed a severe paroxysmal cough with a pronounced whoop while being dressed. The nursemaid had noticed the disappearance of a small safety-pin. When I used the tongue depressor to see the fauces a violent paroxysm was induced and a small open safety-pin came up onto the tongue and was snatched out by the nurse; whereupon the cough ceased. Where the safety-pin had been lodged for two hours I do not know, but it had produced a very good imitation of whooping cough.

The difficulties in diagnosis come in the *early stage*, or from *mild cases* which never whoop. The blood shows a lymphocytosis which increases with the severity of the disease. The highest white blood count seen in our cases was 167,000. Plate cultures can be taken, but the method of identifying the Bordet-Gengou bacillus is more elaborate than that of identifying the diphtheria bacillus, and is less reliable for diagnosis if negative. During the first week, that is, during the catarrhal stage, positive cultures are generally obtained in 80 per cent of

the cases, in 60 per cent during the second week when the paroxysms begin, and in only about 20 per cent during the third week.<sup>10</sup>

*Bronchopneumonia* is the most dangerous complication, and this is particularly apt to occur in the presence of mixed infections, especially with influenza. A persistent small area of bronchopneumonia or enlarged bronchial lymph glands—detected by the *x*-ray—may cause the cough to be protracted over many weeks. Any acute upper respiratory infection, such as a common cold, occurring within three to six months after recovery may bring on a return of the cough and whoop. Thompson and Greenfield<sup>11</sup> have found that sulfanilamide in the usual prophylactic doses by mouth followed by a maintenance dose had no effect on the paroxysms, but reduced the incidence of bronchopneumonia. Malnutrition often becomes a very serious problem, especially in infants.

One thing should be kept in mind, namely, that the *new-born* appear to lack that relative immunity which they have for measles, mumps, scarlet fever, and diphtheria. Therefore, *every effort should be made to protect them from exposure*. Approximately 80 per cent of all deaths from this disease occur in the first year, and about 95 per cent of the deaths occur in the first two years. Maximum protection is not to be expected until about four months after the completion of the injections of Sauer's vaccine.<sup>12, 13</sup>

**Mumps.**—An early sign of epidemic parotitis is *tenderness near the angle of the jaw*. If mumps is suspected, draw the tips of your first and second fingers with firm pressure over and behind the angle of the jaw on each side. In the early stage of parotid gland involvement the patient will wince as this is done. The openings of the parotid ducts are usually red. It is well to look at the sublingual glands, and to palpate the submaxillary glands, because this virus disease may attack one or all of the salivary glands. Only if the ducts are obstructed by the swelling will the patient experience pain from a swallow of fruit juice; consequently absence of this symptom is not of value. When the submaxillary glands are in-

volved there is a marked double chin, and the edema may spread to the pharynx and even to the larynx. If the sublingual glands become badly swollen the edema may involve the tongue itself.

The blood picture is usually that of a leukocytosis with a relative increase in lymphocytes. In the *differential diagnosis* one must keep in mind those swellings of the parotid which occur after surgical operations. Some of these swellings do not suppurate, while many do so. Oral sepsis in typhoidal and septic states may lead to a parotid abscess with fluctuation and neutrophilic leukocytosis. A prolonged intermittent swelling of a salivary gland with pain on taking food leads one to suspect a calculus in the gland itself or in the duct. In rare instances the parotids are known to swell with each menstruation or pregnancy. Another rarity is Mikulicz's disease in which there is persistent enlargement of the salivary and lacrimal glands with or without lymphatic leukemia, and usually with deficient saliva. It is well to keep in mind that other manifestations of mumps such as pancreatitis, mastitis, ovaritis, orchitis, and encephalitis may sometimes precede, accompany, or follow involvement of the salivary glands.<sup>14, 15</sup> The onset of these complications is sometimes accompanied by chills, and if more than one complication exists at the same time the fever may rise to 106° F.

In closing I wish to remind you that the circumstantial evidence of an exposure to a common contagious disease often serves as an important factor in diagnosis, although at times this factor may lead one astray.

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## CLINIC OF DR. AUBREY O. HAMPTON

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#### ROENTGENOLOGY OF THE UPPER GASTRO- INTESTINAL TRACT

ROENTGENOSCOPY accompanied by *palpation with the gloved hand* is the most important part of the roentgen examination of the gastro-intestinal tract. The improvement of fluorescent screens has added greatly to the accuracy and ease of this type of examination. The new fluorescent screen, when used with a Bucky grid, allows a clarity of vision hardly comparable with the old type of apparatus.

There are, however, details of mucosal lining of the gastro-intestinal tract which still remain invisible by fluoroscopy, and certain small ulcerations and tumor nodules may readily escape visualization, especially if they occur in the overweight or heavy, muscular individual. Furthermore, that which is seen during fluoroscopy cannot be studied in a leisurely fashion due to the inherent danger of overexposure to x-ray.

The taking of roentgenograms during fluoroscopy with the aid of compression cones and the proper barium mixture (*spot films*)<sup>1, 2, 3, 4, 5</sup> is the most outstanding recent contribution to the roentgen study of the gastro-intestinal tract. By these aimed roentgenograms taken instantaneously with controlled compression, the inner relief of the gastro-intestinal tract can be completely and accurately studied in all its macroscopic detail excepting color. Since it is not practical to take these localized films, which are about 3 inches in diameter, of the entire organ to be examined, it of course follows that the examiner must be expert in the use of the fluoroscope. He must first discover evidence of disease before he can "aim"

the "camera." Obviously, one cannot aim at a target which is not visible, but a roentgenogram of the suspected site of disease may at times reveal clearly a lesion which was not seen during fluoroscopy.

The *technic* of the study of the mucosa of the gastro-intestinal tract is also dependent upon the *proper mixture* of contrast substance. It has been found necessary to use heavier suspensions of barium in water than was heretofore thought necessary, the proportion of barium to water being equal by volume.

**Esophagus.**—By the use of the above-mentioned improvements in technic and as a result of the stimulus to closer observation of the mucosal pattern of various organs of the gastro-intestinal tract, Wolf<sup>6</sup> and Schatzki<sup>7</sup> were able to demonstrate *dilated veins* or *varices* in the esophagus. The demonstration of varices is important because of the frequency of this finding in patients with portal obstruction, particularly cirrhosis of the liver. This is well illustrated by the following case report:

**Case I.**—A male, aged fifty, entered the hospital with chief complaint of weakness, malaise and loss of weight. Four years before entry he had noted tarry stools on one occasion. Weakness had been noted for one month during which time he lost 20 pounds in weight. On physical examination a mass was noted in the epigastrium slightly to the left of the midline, which was thought to represent a tumor of the gastro-intestinal tract. On roentgen examination the mass in the epigastrium was seen to be typical of an enlarged spleen situated unusually far toward the midline. The esophagus showed extensive varices throughout its whole thoracic portion (Fig. 170).

**Stomach.**—The differential diagnosis of *ulcerating lesions* of the stomach still remains a difficult problem. A grossly malignant lesion can be readily recognized roentgenologically, but certain malignant ulcerations which appear grossly benign to the surgeon and pathologist present the same characteristics to the roentgenologist. The effect of diet on the roentgen appearance of the ulcerating lesion is still a valuable aid in the differential diagnosis, but even this time-honored method has been found unsafe in an alarming number of cases.

All ulcerating lesions in the stomach are looked upon with increasing suspicion as more careful histologic studies are done. The possibility of error on the part of the pathologist in the study of these ulcerations is much higher in those cases reported as *benign* than in those reported as *malignant*. When the pathologist states that a lesion is carcinoma, there need be little doubt; but when he expresses an opinion that the lesion is benign, there is always the possibility that the section which



Fig. 170 (Case I).—Varices of the esophagus in a case of cirrhosis of the liver. The rounded and cylindrical filling defects represent dilated veins.

he studied did not include the malignant portion of the lesion. The malignant tissue is often partially ulcerated away or very small, and for these reasons the taking of serial sections of grossly benign lesions in the stomach is gradually becoming a routine procedure.

**Prepyloric Ulcers.**—Although grossly benign but histologically malignant ulcerations may occur in any portion of the stomach, it has been found that they are much more frequent in the immediate prepyloric area, or distal 1 inch of the stomach.<sup>5</sup>

Ulcerations in the prepyloric area, although quite small and showing the gross characteristics of benign lesions and even a response to ulcer diet, *should be considered malignant* until proved benign by serial histologic examination. This fact is illustrated by the following two cases:

Case II.\*—A forty-eight-year-old woman entered the hospital complaining of epigastric discomfort. Ten years before she had gone to her physician with symptoms of constipation and fatigue. Two years later she complained of epigastric fulness which often woke her at night. x-Ray studies were negative. When seen four years later, approximately four years before entry, she was complaining of indigestion which was sometimes relieved by food, soda,



Fig. 171 (Case II).—A typical prepyloric ulceration is seen just proximal to the pyloric valve in the distal 1 inch of the stomach.

or belching. Seven months before entry she was well except for epigastric discomfort which often awoke her at 2:00 A. M. A few weeks before entry, following a rough sea voyage associated with seasickness, there was epigastric gnawing; this was relieved temporarily by food but it persisted several days. The physical examination and all laboratory examinations except the x-ray were negative. An ulcerating lesion was found in the prepyloric area of the stomach, as shown in Fig. 171.

Four days after the x-ray examination an exploratory laparotomy was performed and a small area of flexible thickening was found just proximal to the pylorus. The surgeon doubted the presence of an ulcer and, because the

\* Reported in the case records of the Massachusetts General Hospital; Case No. 2111, March 14, 1935, New England Journal of Medicine.

x-ray examination was so recent, thus eliminating the possibility of healing by diet, the surgeon considered it unwise to do a resection. It was thought that follow-up x-ray studies would be a more reasonable procedure than excision.



Fig. 172 (Case II).—Examination nine weeks later shows no evidence of prepyloric ulceration.

x-Ray examination three weeks after operation showed no change, and another examination nine weeks after operation revealed that the ulcer crater had disappeared (Fig. 172), but that the indurated area (Fig. 173) persisted. The



Fig. 173 (Case II).—Spot film of the antrum of the stomach shows thickening of the mucosa at the site of the previous ulceration.

induration could be demonstrated by failure of the peristaltic waves to pass over the lesser curvature and by the absence of normal gastric rugae in this region.

Because of the persistent x-ray findings a second operation was performed, the pylorus being resected. At this operation the ulceration in the prepyloric area was not demonstrated either by the surgeon or the pathologist. The operative specimen is illustrated by the artist's drawing (Fig. 174). The artist has exaggerated the abnormal changes noted. The pathologist had difficulty in visualizing any lesion even after the stomach was open. Serial sections were made of the entire prepyloric area. These histologic preparations showed an



Fig. 174 (Case II).—Artist's drawing of surgical specimen. The variations from the normal are exaggerated. Note convergence of mucosal folds toward what appears to be a healed gastric ulcer.

abnormal area of highly atypical cells over an area 1.5 cm. in diameter. Mitotic figures, which are of course normal in the gastric mucosa, were increased four to five fold over the usual number. There was no trace of invasion of the surrounding areas of the stomach and, for this reason, the lesion was diagnosed as "carcinoma in situ." The specimen was shown to a great many pathologists and the average was three to one in favor of malignancy.

**Case III (U 77452).**—This patient, a man aged forty-four, entered the hospital complaining of pain in the epigastrium, hematemesis and black stools. The pain in the epigastrium began eight months before entry; was intermittent in character, sharp and crampy; and was present before and after meals. The pain was relieved by soda but was not noticeably improved by food. Three weeks before entry the patient noticed black stools which continued until time of admission. One week before entry he vomited following a bout of pain, and one day before entry he again vomited and raised some bright red blood. He fainted while waiting to be admitted to the hospital. His bowels had been irregular and his appetite poor. He had lost 30 pounds in weight.

Roentgen examination revealed an area of ulceration on the lesser curvature at the pyloric valve (Fig. 175). This lesion was 1 cm. in diameter and about 1 cm. in depth, and appeared to be benign. The second roentgen ex-

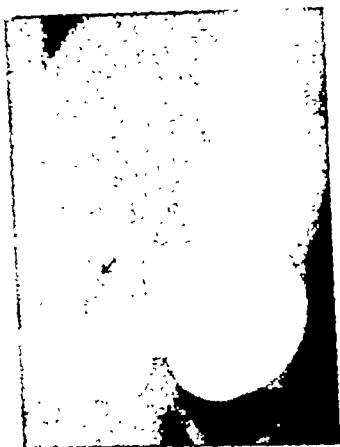


Fig. 175 (Case III).—There is a 1 X 1 cm. ulceration on the lesser curvature side of the pyloric valve which appears benign.



Fig. 176 (Case III).—Examination twenty days later shows definite reduction in the size of ulceration.

amination twenty days after the first (Fig. 176) showed the ulceration to be but one-half as large as before. There was no definite obstruction.

The patient was discharged with a diagnosis of benign pyloric ulcer, but he returned within one week because of persistent vomiting. One liter of



gastric contents was aspirated on entry. At operation, one week after the second examination, "a large, indurated ulcer which traversed the pyloric muscle of the stomach was found." It was thought to be questionably malignant and a radical gastrectomy was performed. The pathologist described the ulceration as occupying the pyloric valve and measuring 1 cm. in diameter and 1.5 cm. in depth. It was hard and indurated for a distance of 1 cm. on all sides. A number of glands were found in the adjacent mesentery which measured up to 1 cm. in diameter. The histologic diagnosis was carcinoma of the pylorus with secondary peptic ulceration and metastases to one regional lymph node.

Sampson and Sosman<sup>9</sup> presented a number of cases similar to the above and they concluded that "prepyloric ulcers which do not disappear completely within a few weeks should be treated by radical resection, and even those that disappear should be carefully followed and re-examined periodically." They also found that 75 per cent of prepyloric ulcerations eventually show evidence of malignancy on serial section.

It has been the custom in the Massachusetts General Hospital for seven years to consider prepyloric ulcerations as *malignant until proved otherwise*, and it has been almost a routine procedure to refer these patients to the surgeon for operation. The few cases which have been followed on ulcer regimens have not been tabulated. The frequency of malignancy in those ulcerations which completely disappear when the patient is on an ulcer diet has not been established.

There are instances of benign ulceration in this area and they probably amount to a fair number. It is thought that ulcer occurring anywhere in the stomach should be viewed with suspicion, re-examined frequently and at the slightest suggestion of malignancy, promptly resected. Benign gastric ulcer as diagnosed by roentgen examination is a relatively rare lesion; its infrequency prevents accurate statistical data.

**Bleeding Duodenal Ulcer.**—Peptic ulcers of the stomach and duodenum frequently produce massive hemorrhage, but they may heal so completely within three weeks that they cannot be visualized by x-ray (Fig. 177, *a* and *b*). Any ulceration in the stomach or duodenum, in fact, may heal completely within this period of time and, if there is no residual deformity

of outline due to scarring, the  $x$ -ray examination may be entirely negative. For this reason the examination should be made before a prolonged ulcer diet has been tried. Furthermore, it is necessary to rule out neoplasms such as *leiomyoma*, *sarcoma* and *carcinoma* as a cause of bleeding as soon as possible.

The  $x$ -ray examination of patients suffering from acute hemorrhage is usually deferred until the hemorrhage has been checked by diet or medication, because palpation and manipu-

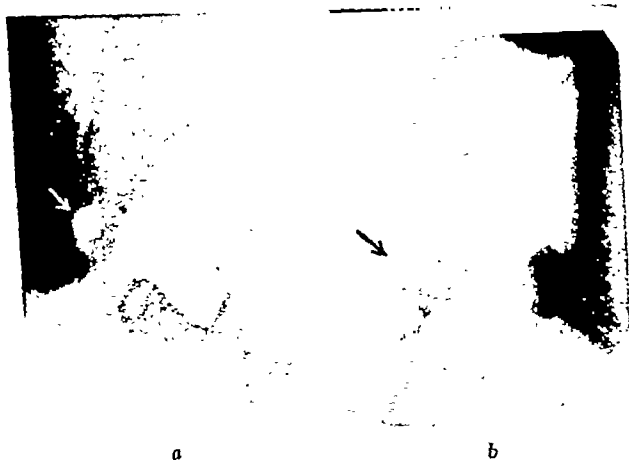


Fig. 177.—*a*, Active anterior wall duodenal ulcer. *b*, Same case a few weeks later showing complete healing of ulceration and no deformity of the duodenal cap.

lation of the viscera are considered dangerous while the lesion is bleeding. It has been demonstrated, however, that examination of the patient *before the end of the first week or ten days* is of definite value in the establishment of the correct diagnosis and that this examination can be made without danger to the patient.<sup>10</sup> It is done in the horizontal position without palpation and with the use of a thick barium mixture and "spot films" during fluoroscopy. Such examinations are particularly valuable in the study of bleeding posterior wall duodenal ulcers. The patient is given a few swallows of thick barium suspension

as he lies upon the fluoroscopic table. He is turned on his right side and maintained in this position until the duodenum is completely filled; then by simply rotating the patient back to the left side under fluoroscopic control an ulcer crater on the posterior wall of the duodenum can be readily demonstrated (Fig. 178).

**Gastritis.**—With the development of interest in gastroscopic examination and  $x$ -ray study of the mucosal relief, gastritis has become a common diagnosis. Thickened and irregular mucosal folds, together with retained secretions in the stomach, are considered sufficient  $x$ -ray evidence for a diag-

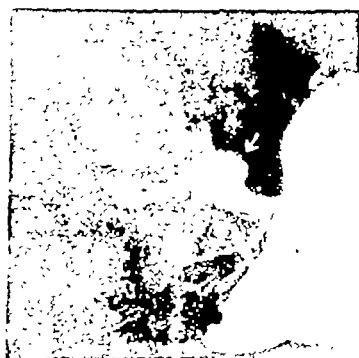


Fig. 178.—An ulcer of the posterior duodenum demonstrated with patient in horizontal position without palpation or compression.

nosis of gastritis, but many patients suffering from severe gastritis and bleeding show no disease on  $x$ -ray examination (Fig. 179). Bleeding gastritis without peptic ulcer or tumor is an accepted clinical fact, and in some cases this bleeding may be so severe as to require radical surgery.

*Localized hypertrophic gastritis* is of importance clinically and radiologically because it may be mistaken for carcinoma of the stomach. A differential diagnosis can usually be made by gastroscopic examination and careful  $x$ -ray study. The  $x$ -ray picture is that of large cylindrical filling defects arranged in a twisted mass, usually on the greater curvature and above the middle of the stomach. These large mucosal folds are

flexible, and complete filling of the stomach usually obliterates the deformity.

**"Hiatus Hernia."**—Herniation of the stomach through the esophageal hiatus is much more common than gastric ulcer in middle life and even more common than duodenal ulcer in the sixth or seventh decades of life. In fact, "hiatus hernia" is present in such a high percentage of elderly patients that it is probably a normal finding. The roentgen appearance and



Fig. 179.—Normal mucosal relief of the upper two thirds of the stomach in a patient suffering with severe gastritis as demonstrated by gastroscopic examination.

incidence of these hernias was first pointed out by Morrison and Healy in 1925.<sup>11</sup>

In 1932 Schatzki<sup>12</sup> made careful studies of thirty patients past the sixth decade of life, giving particular attention to the incidence of hiatus hernia. In this series of cases he found fourteen hernias, and eight additional cases were shown to have similar hernias when the intra-abdominal pressure was increased by the insufflation of air in the colon. Thus, in a group of thirty elderly patients, twenty-two were found to have

hiatus hernias. Schatzki argued that these hernias develop in much the same manner as other hernias, that increase in intra-abdominal pressure is an important factor, and that they are not congenital.

The large hiatus hernias with "upside-down stomach" should not be confused with this type of hernias. In fact, the *diaphragmatic hernia* which remains filled when the patient is in the upright position probably should be separated from this group. The *common type* of hiatus hernia is small, does



Fig. 180.—Common type of small hernia of the fundus of the stomach through the esophageal hiatus of the diaphragm.

not usually remain filled when the patient is upright, and cannot be demonstrated satisfactorily except by filling the esophagus when the patient is in the supine position. The diagnosis is simple when the proper technic of examination is observed (Fig. 180). The mucosal folds of the herniated portion of the stomach are similar to those of the remainder of the fundus, in contrast to the thin mucosal markings of the esophagus.

That small hiatus hernias produce *symptoms* in some patients is emphasized by Bock<sup>13</sup> and Jones.<sup>14</sup> Occasionally the

mucosa in the herniated portion of the stomach is markedly thickened and may be the source of serious bleeding. A variety of symptoms may be produced by the common hiatus hernia, such as vomiting, epigastric pain referred to the back, or a radiating pain referred up the left arm and simulating angina. Symptoms from this condition are rare, however, and usually develop after middle life following a rapid gain in weight.

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### FEVER THERAPY IN DISEASES OF THE NERVOUS SYSTEM

TEN years have elapsed since the introduction of artificial fever therapy by mechanical methods. Its chief application lay in the realm of neuropsychiatric disorders due to syphilis, and its aim was to replace malarial therapy which, during the preceding decade, had already proved its usefulness. Fever therapy soon spread to the sphere of other nervous diseases and also to many other medical conditions. Its value in the latter conditions with few exceptions has not been very great. Owing to popularization of the method, a fair evaluation of the treatment of neuropsychiatric disorders has become clouded. It is therefore fitting to review the subject of fever therapy in relation to diseases of the nervous system: its usefulness, limitations, contraindications, therapeutic results, and mechanism of action.

#### HISTORICAL CONSIDERATIONS

The origin of fever therapy is attributed to Wagner-Jauregg who, in 1887, suggested the beneficial effect of febrile diseases upon certain psychotic conditions.<sup>1</sup> It was not until 1917, however, that he was able to utilize this idea in the actual treatment of patients, and in that year he gave malaria



inoculations to patients with parietic neurosyphilis. The results were immediately very striking, and the apparent antagonism between malaria and neurosyphilis became emphasized. A recent study by Needles<sup>2</sup> clearly illustrates this point. Of about 12,000 patients in the tropics, he found that 31 per cent were syphilitic and, of these latter patients, only one had neurosyphilis and had never had malaria. Other fever-producing agents were employed by numerous co-workers of Wagner-Jauregg and by other workers in this country. These included *staphylococcus vaccines*, *old tuberculin*, *relapsing fever*, *sodium nucleinate*, *milk injections*, *typhoid vaccines*, and *rat-bite fever*. The opinion grew that the mechanism of action of these therapeutic agents was nonspecific foreign protein shock. Although this matter has never been settled, malarial fever was held to be the most efficacious in the treatment of parietic neurosyphilis.

Since elevated temperature was the common denominator in all these forms of nonspecific therapy, attention was focused, particularly in this country, upon the production of hyperpyrexia without the use of infectious agents. Thus experimentation with physical agents began to be made. The first attempts utilized the principle of *high-frequency diathermy*, and two clinical investigations were going on simultaneously in 1929, published by Neymann and Osborne and by King and Cocke.<sup>3</sup> After extensive animal experimentations, diathermy was applied to patients with parietic neurosyphilis in a number of other clinics in this country. At about the same time Carpenter *et al.*<sup>4</sup> found that hyperpyrexia could be produced by *radiotherapy*, and this method enjoyed a brief vogue in the treatment of patients. These two methods utilized the principle of internal heat in the production of hyperpyrexia.

Attention was soon directed to the principle of *external heat*, and methods employing hot baths, hot air, infrared and carbon-filament light cabinet, and the electrical blanket have been successful in producing hyperpyrexia. In 1934, investigations with an air-conditioned cabinet (*Kettering hypertherm*) were started and subsequently the method was tried

out in various institutions in this country. Since then the principle of circulating hot, humid air has been used extensively for the production of hyperpyrexia, almost to the exclusion of all other methods of mechanical fever therapy. Malaria, however, has not been replaced.

Considerable disparity has existed in regard to the therapeutic results of these various methods in neurosyphilis. Some workers, particularly Wagner-Jauregg, have felt that there was something specific in malaria which stimulated immunologic reactions leading to cures. Still others obtained even better results by the use of mechanically induced fever.

#### PARETIC NEUROSYPHILIS

**Malaria Therapy.**—The most definite place for artificial fever is in the treatment of paretic neurosyphilis. Malaria is well established throughout the world as standard treatment for this disorder. The extensive clinical studies of Wagner-Jauregg and his Viennese school and the statistical data obtained in many of the clinics in this country show that about a third of the patients have complete and lasting remissions. An additional third of the patients achieve a partial remission; the remainder are unimproved. The mortality rate, which in untreated cases is practically 100 per cent, is greatly reduced and the longevity is greatly increased. Malaria in itself carries a mortality rate which varies greatly in different clinics, but in our experience the rate, figured rather liberally, is approximately 3 per cent.

During the past fifteen years much work has been done with malaria treatment in the Boston Psychopathic Hospital. Treatment with sodoku (rat-bite fever) originated in this clinic, and typhoid vaccine therapy has also been employed.

**Mechanically Induced Fever Therapy.**—In 1931 *electro*pyrexia was begun in the treatment of paretic neurosyphilis, and various forms of mechanical fever have been employed: diathermy, electric blanket, circulating hot, moist air, radiant energy cabinet, and inductothermy. As a result of these experiences the impression was gained that malarial therapy

yielded better results than the other febrile methods. There appeared to be no consistent correlation between the amount and height of the fever and the clinical results. The same situation applies to malarial therapy.<sup>5</sup>

**Comparison of Results by the Two Methods.**—There are some statistical data, notably those of Bunker and Kirby, and Ferraro and Fong,<sup>6</sup> which tend to show the *optimum number* of paroxysms of malarial fever that produces the best therapeutic results. They found also that clinical improvement seemed to parallel the height of temperature and the number of paroxysms experienced. On the other hand, there are some good results reported in the literature with a relatively small number of malarial paroxysms at lower temperature levels. Wagner-Jauregg originally emphasized this point by citing instances of recovery of patients treated by vaccine therapy without febrile reactions.<sup>7</sup> He repeatedly calls attention to the fact that relief followed the use of various forms of nonspecific foreign protein shock, and further that recoveries occurred in patients treated by malaria without developing fever. Consequently Wagner-Jauregg has consistently objected to the use of electropyrexia in the treatment of parietic neurosyphilis and sums up his arguments in two recent papers.<sup>8</sup>

Comparative studies of the results of malarial therapy and mechanical hyperpyrexia are difficult to evaluate owing to the fact that there are hardly two groups of cases in the literature that are comparable with each other. Many *variants* enter into consideration, such as the exact type and amount of follow-up treatment, the selection of patients, and the length of time the patients were followed before the report was made, not to mention the personal equation which enters into the conclusions made. Nevertheless a perusal of the statistical data reported in the literature leads one to conclude that the *percentage* differences are but slight:

In a survey made in 1935 of over 3,000 patients treated by *malaria*,<sup>9</sup> the percentage of good remissions varied from 20 to 41, and partial remissions ranged widely up to 50 per cent. Neymann<sup>10</sup> quotes Kraepelin's compilation of more than 3,000

cases, with improvement in approximately 43 per cent. With regard to *mechanical hyperpyrexia*, Neymann's records in a series of nearly 1,000 cases show complete remissions in 27 per cent and partial improvement in 36 per cent. This corresponds with our own figures of 27 per cent and 40 per cent for good and partial remissions, respectively.<sup>5</sup>

#### Indications for Mechanically Induced Fever Therapy.

—Despite the enthusiasm of many authors regarding the superiority of mechanically induced fever therapy, it may be fairly stated that the actual results do not appreciably surpass those obtained in malaria-treated cases of paretic neurosyphilis. The logical question then is, What are the indications for mechanical hyperpyrexia in this disease?

That fever is a most potent therapeutic agent is established by the many reports in the literature and is clearly demonstrated by some clinical experiments recorded in 1936.<sup>11</sup> A group of twenty-one patients, who represent therapeutically recalcitrant cases in our tryparsamide-treated cases, were subsequently subjected to fever therapy. In almost every instance the results obtained after fever were good, both clinically and serologically. While most of these patients received malaria, there is a reasonable assumption based upon the extensive experience of many workers that similar results follow mechanical hyperpyrexia.

Although we cannot subscribe to the opinion that *electro-pyrexia* yields superior results, there is a definite place for this form of fever in the treatment of paretic neurosyphilis. Some patients, especially of the *colored race*, who present themselves for treatment are immune to malaria. Moreover there are definite *contraindications to the use of malaria*: namely, cardiac and renal diseases and other debilitating conditions. Such patients can be given mechanical fever with less danger to life. Furthermore, for the purpose of giving a second course of fever to patients who previously received malaria, electropyrrexia is a useful substitute. It is not to be presumed that malaria has been replaced by electropyrrexia, but rather that the latter is an adjuvant to the armamentarium of the neurosyphilologist.

**Tryparsamide.**—It is frequently stressed in the literature that fever therapy should always be followed by antisypilitic drugs, and that the best therapeutic results are obtained by a *combination* of fever and chemotherapy. The most important drug in this group is tryparsamide. In this connection two statements may be emphasized: that treatment with tryparsamide is capable of producing beneficial results similar to those produced by malarial therapy,<sup>12</sup> and that a considerable number of preliminary tryparsamide injections greatly enhances the probability of therapeutic success in the treatment of parietic neurosyphilis.<sup>11</sup>

#### TABETIC NEUROSYPHILIS

**Malaria Therapy.**—The therapeutic effect of fever upon the course of tabes dorsalis is not so striking. Because the effectiveness of malaria was demonstrated in patients with parietic neurosyphilis, it was applied to tabetics. Although serologic reversal was frequently accomplished, clinical cures were not readily forthcoming.

Improvement in these cases is difficult to evaluate because of the great variety of symptoms. Statistical evaluation of malaria-treated cases cannot be satisfactorily made upon the basis of the relatively small number of cases reported in the literature. In a series of about twenty cases we have not seen such spectacular results as some authors have reported.<sup>13</sup> In our experience, the ataxia and lightning pains are often worse after treatment. Moreover, tabetics with cord bladders are prone to develop serious complications due to infection. We have obtained some relief in patients with *gastric crises*. In *optic atrophy*, malaria is of distinct value in arresting the progress of visual loss. Moore<sup>14</sup> obtained a favorable result in 39 per cent of the patients and contrasts this figure with the 54 per cent good results of subdural treatment. In our experience with malaria therapy in tabes, about half the cases were arrested or improved.

**Indications for Fever Therapy.**—On the basis of all available information there seems to be definite indications for

the use of malaria in tabes, as follows: (1) when parietic neurosyphilis coexists, (2) in patients with optic atrophy, (3) as treatment for gastric crises unrelieved by other means, and (4) in any tabetic with spinal fluid reactions (paretic formula) resistant to prolonged treatment. The same criteria hold for the use of *mechanical* hyperpyrexia.

**Comparison of Results of Malaria and Mechanical Hyperpyrexia.**—Neymann, in his book, gives a compilation of the clinical results obtained by mechanical hyperpyrexia in 114 cases reported by several authors. Sixty-six per cent of the patients are considered clinically improved, but no mention is made of the degree of relief from specific symptoms. In our own experience with about thirty cases, the therapeutic results have not been appreciably better than those from malaria.<sup>15</sup> However, it must be pointed out that the lightning pains and gastric crises disappear during the course of an individual fever bout, even though recurrences are not necessarily prevented. Some excellent results, as have been indicated, have been observed in cases of optic atrophy. In fact artificial fever therapy is the method of choice in this condition. In one instance of Charcot joints, an arrest of the process occurred.

#### MENINGOVASCULAR NEUROSYPHILIS

**Indications for Fever Therapy.**—The indications for fever therapy in the meningovascular varieties of neurosyphilis are not definite. These conditions are milder forms of neurosyphilitic involvement and more readily respond to antisyphilitic treatment than do the parenchymatous disorders, tabetic and parietic neurosyphilis. Excellent to good results are obtained in about 80 per cent of the cases. Various observers, notably Ebaugh, and Wile and Davenport<sup>13</sup> in this country, have reported approximately the same results in patients treated by *malaria*. Having in mind the great efficacy of tryparsamide in all forms of syphilitic involvement of the nervous system, it would seem wiser to reserve malaria treatment in the meningovascular cases until at least a year's treat-

ment of chemotherapy has demonstrated failure to bring about serologic improvement. In other words, if a patient with meningovascular neurosyphilis fails to improve, and especially if the spinal fluid shows the paretic formula, malaria should be given as prophylaxis for the future.

In *early* meningeal syphilis, neither tryparsamide nor fever therapy is advisable at the start of treatment, but they may be used after two to three years' of treatment in patients with resistant spinal fluid serology. The treatment of *vascular* neurosyphilis is not so successful. Only about a third of the patients show good results. Malaria is *contraindicated* on account of the deleterious effects upon the circulatory system. When the focal vascular lesion is associated with paresis, the risk from fever therapy must be accepted in view of the gravity of the situation. In such instances electropyrexia is to be preferred. There are no special advantages in this form of fever therapy, except the value of controlling the height and duration of the induced fever in patients whose cardiovascular system is severely taxed. Our own experience as well as that of others<sup>14</sup> bears out this point.

#### ASYMPTOMATIC NEUROSYPHILIS

**Prophylaxis.**—The prophylaxis of neurosyphilis lies in a study of the spinal fluid reactions. This involves the diagnosis of asymptomatic neurosyphilis, which is the forerunner of late graver manifestations of neurosyphilis. These may be prevented by appropriate treatment in the early asymptomatic states. The importance of *early diagnosis* is obvious. However, in spite of active, vigorous chemotherapy, early asymptomatic neurosyphilis progresses to active neurosyphilis in about 3 to 8 per cent of the cases.

**Malaria Therapy for Resistant Cases.**—It is this group of resistant cases that requires fever therapy. O'Leary,<sup>16</sup> on the basis of a study of eighty-nine cases of asymptomatic neurosyphilis treated with malaria, obtained a high percentage of serologic reversals. This procedure was originally used in the

Viennese clinic shortly after the demonstration of its value in general paresis. The experience of many observers, summarized by Matuschka and Rosner,<sup>17</sup> shows results up to 100 per cent. While our experiences do not reach such perfect results, we believe that malaria should be given to patients of this type after they have had considerable chemotherapy.

**Mechanical Hyperpyrexia.**—Accumulated clinical evidence indicates that fever therapy adequately prevents clinical neurosyphilis. It had been noted that patients who received adequate chemotherapy and later malaria treatment showed no clinical progression, whereas those who received inadequate amounts of arsenicals and heavy metals prior to fever therapy showed progression to the serious manifestations of parenchymatous and meningovascular neurosyphilis. Thus within recent years, mechanical hyperpyrexia has been employed in asymptomatic neurosyphilis.

The literature contains reports of small numbers of cases in which serologic improvement is always uniformly satisfactory.<sup>10</sup> Whether or not electropyrrexia has a greater therapeutic efficiency is a matter of opinion. Our own experience indicates that serologic reversal is sometimes extremely difficult. We conclude, therefore, that the best method of treatment of resistant asymptomatic neurosyphilis is *combined artificial fever therapy and chemotherapy*.

#### JUVENILE PARESIS

The results of fever therapy in cases of juvenile paresis are not so favorable as in the acquired disease. The literature contains several reports with but few good remissions following malaria treatment. Our own experience with this disease has yielded unsatisfactory results. This was also true of treatment with electropyrrexia. Neymann, in his book, also reports disappointing results. Menninger<sup>18</sup> states that the best therapeutic results are obtained by a *combination of fever, arsenicals, particularly tryparsamide, and heavy metals*, continued over a very long period of time. Review of the literature shows that about 10 per cent of the patients were markedly improved.



Although the number of patients treated by *electropyrexia* is small, there would appear to be a higher percentage of good results in this group than in that treated by malaria.

#### INTERSTITIAL KERATITIS

The literature<sup>19</sup> indicates that interstitial keratitis in its acute inflammatory state is greatly helped by fever therapy. We have observed excellent results in fourteen cases treated by electropyrexia in the Boston Psychopathic Hospital Clinic. Many favorable reports have likewise appeared on the value of malaria treatment of interstitial keratitis, with and without evidences of neurosyphilis. Whether malaria or electropyrexia is to be preferred is not clearly established.

Although interstitial keratitis is a relatively rare concomitant of juvenile paresis or of congenital neurosyphilis, the effect of fever as a precipitating factor has recently been pointed out.<sup>20</sup> The occurrence of interstitial keratitis with a relatively high frequency following treatment is the reason for including this disease in the present discussion. In a series of thirty cases of juvenile paresis, three patients developed interstitial keratitis subsequent to fever treatment and while receiving arsenical treatment, and four patients of the series of nine cases of nonparetic congenital neurosyphilis, who were not given fever therapy, likewise developed interstitial keratitis. This would appear to be more than a coincidence. The hypothesis is advanced that the febrile condition enhances the possibility of the appearance of an interstitial keratitis (a gummatous lesion) in a patient with an essentially parenchymatous disease.

#### NEURITIS

The relief of neuritic pains following artificial fever therapy has been emphasized by Bennett and Cash,<sup>21</sup> who had previously reported upon the outstanding relief of intractable pains in tabes dorsalis. Considerable clinical evidence (forty cases) is presented that artificial hyperpyrexia is a valuable therapeutic aid in relieving painful neuritic, myalgic, menin-

gitic and radicular states. However, other forms of treatment were also employed in conjunction with fever, and it is stated that fever therapy is merely an *additional aid* in the management of the patients.

The conditions treated include sciatica, brachial neuritis, infectious polyneuritis, herpes zoster, radiculitis, and neuritis secondary to arthritic disease. We have had but little experience with fever therapy in these conditions, but we are not convinced that it has any specific value beyond the local effects of heat.

### MENINGOCOCCAL INFECTIONS

Moensch<sup>22</sup> observed that the meningococci react to heat *in vitro* much as do the gonococci. Hence artificial fever therapy would be expected to have as favorable an effect upon meningococcal as upon gonococcal infections. Bennett *et al.*<sup>23</sup> treated two cases of chronic meningococcus septicemia with meningitic recurrences and obtained cures in each. In four patients with chronic meningococcic meningitis, clinical improvement followed fever therapy alone. Bennett therefore recommends fever as an adjuvant therapy in subacute or chronic cases, which do not respond to serum or drug therapy.

However, with the advent of *sulfanilamide* and related compounds and the striking therapeutic results obtained thereby in both meningococcic and gonococcic infections, there would seem to be little use for fever therapy in these diseases. The treatment of gonococcal arthritis, which responds very well to mechanical fever therapy, is not here discussed since it is not a disease of nervous origin.

### MULTIPLE SCLEROSIS

Any treatment for such an intractable disease as multiple sclerosis is greatly desired. Therefore, despite the fact that malarial therapy had proved to be useless, artificial hyperpyrexia by mechanical means was tried. Schmidt and Weiss<sup>24</sup> were the first to use this method. Later Schmidt states that he had treated over 100 patients, with results varying from

complete remission to marked improvement. These data cannot be statistically evaluated. However, in Neymann's book there is a statistical analysis of some fifty cases, the majority being his own, in which 69 per cent of the patients showed improvement following electropyrrexia. He states guardedly that not enough time has elapsed since electropyrrexia was introduced to warrant far-reaching conclusions regarding the ultimate prognosis. Moreover, in bold type, the statement is made that *electropyrrexia is not a cure for multiple sclerosis*. Weiss has reported the largest group in the literature (144 cases) with improvement in 65 per cent.

Our own observations in nineteen cases treated by *electropyrrexia* were not so encouraging, only two patients in the group being considered improved. It is extraordinarily difficult to evaluate symptomatic improvement in this disease because there is a strong tendency toward natural remissions followed by recurrences. Furthermore most patients are euphoric and optimistic, and are likely to report improvement under any therapy. On the whole there is no objective evidence of improvement that can definitely be attributed to fever, and there is an equal chance that the patient will become worse. The work of Putnam would almost preclude the expectation of favorable results from artificial fever therapy in this disease.<sup>25</sup>

#### SYDENHAM'S CHOREA

The results reported in the treatment of Sydenham's chorea have been on the whole very satisfactory. We have had the opportunity to treat only one case, with prompt and complete cessation of choreiform movements. Five different groups of investigators<sup>26a</sup> have reported on 167 cases with a very high percentage of recoveries and but few recurrences. Each of the investigators has found that complicating carditis is not a contraindication to use of fever therapy, but on the contrary, reports improvement in this condition. Nonspecific foreign protein shock therapy preceded the use of *electropyrrexia* and appreciably shortened the duration of the attacks.<sup>26b</sup>

In general, the results obtained by foreign protein therapy have been about the same as by electropyrrexia. Thus there can be no doubt about the value of fever therapy in this disease. Whether artificial fever produced by physical agents is the treatment of choice is merely a matter of opinion. However, there is considerable clinical evidence that many patients make excellent recoveries under ordinary treatment without fever.

#### MISCELLANEOUS NEUROPSYCHIATRIC DISORDERS

**Toxic-infectious Psychoses.**—Bennett<sup>23</sup> reports on five cases, classified as toxic-infectious psychoses, treated by means of artificial fever therapy with good results. It was his impression that the fever treatment shortened the usual period of hospitalization in these cases. However, from the data available on this subject, no definite conclusion can be drawn.

**Other Organic and Functional Disorders.**—Fever treatment of other organic nervous disorders, such as *chronic epidemic encephalitis*, *lobar sclerosis*, and *cerebral arteriosclerosis*, was also tried without success. A variety of other psychotic states of a functional nature—*depressions*, *excitements* and *stupors*—failed to respond to fever therapy.

It is worthy of mention that the initial impetus in the clinical utilization of artificial fever therapy came out of repeated observations of remission and recovery phenomena in nervous and mental disorders following *spontaneous* intermittent fevers. These observations were first made in the *functional psychoses* and in *epilepsy*. Reports relating to the latter condition date from the time of Hippocrates. Observations of the effect of intercurrent natural fevers upon the functional psychoses have been reported since the middle of the nineteenth century. However, the earliest attempt at the clinical use of artificial fever was made in 1876 by Rosenblum of Odessa, Russia. His results were practically unknown until Oks<sup>27</sup> published a translation of them in a German periodical in 1880. A few years later Wagner-Jauregg published his observations concerning the beneficial effect of fever on mental

disease and particularly on neurosyphilitic disorders, which paved the way for the subsequent use of artificial fever therapy.

In a recent monograph, Terry<sup>28</sup> made a survey of the literature and current opinion on the effects of fever upon the *functional mental disorders*. Many types of fever-producing agents were included in this study: malaria, typhoid vaccine, sulfur-in-oil, and electropyrexia in its various forms. Upon the basis of extensive numbers of case reports, the conclusion is reached that in the *affective* psychoses, the value of fever is either negligible as a general therapeutic agent or that the somewhat vaguely described recoveries were coincident with spontaneous improvement. In the *schizophrenic* psychoses, interpretation of results attained have been widely controversial. The impression gained from the various articles is that the method may be followed by remissions, especially in acute and recent cases in which spontaneous remissions are common, but that its use alone cannot effect a material increase in the recovery rate of schizophrenia. The results of artificial fever therapy in *epileptics* are not particularly encouraging. Such treatments are rarely reported to exert more than a temporary subsidence of seizures, and may be attended by dangers.

#### MECHANISM OF FEVER THERAPY

The mechanism of action in induced fever is not clearly known. Many theories have been propounded, and to a large extent they have been uncritically influenced by contemporaneous medical enthusiasms and specialized individual interests. During the latter part of the nineteenth century, the majority opinion attributed the beneficial effects of fever upon psychotic conditions to supposedly induced *circulatory* and *nutritional* changes in the central nervous system. Other views consider the beneficial results observed to be largely, if not entirely, *psychological*.

Recent hyperpyrexial studies have tended to emphasize certain physiological aspects: They suggest that fever produces a variety of reactions: (1) it mobilizes and enhances the efficacious action of certain body defense mechanisms, (2)

effects significant changes in the functioning of the autonomic nervous system, and (3) inhibits the development and growth of the invading organisms. It is difficult to determine the effect of such bodily activities and their emotional components upon the psychic state, and conversely, to comprehend the action of such emotional changes on physiological processes.

**Neurosyphilis, Meningococcic Infections, and Multiple Sclerosis.**—In *neurosyphilis*, there are three outstanding factors relating to the mechanism of artificial fever therapy. One is the destruction of the invading spirochetes caused by elevation of body temperature. Another is the biologic response to nonspecific foreign protein shock. Some investigators believe that the therapeutic effect is due to a combination of the fever and its accompanying biologic reaction. Moreover, there is some evidence that malaria stimulates the reticulo-endothelial system. The third factor, staunchly supported by Wagner-Jauregg, is the alteration produced in the brain parenchyma by the malarial organism. It has been shown that there is a transformation of the parietic type of process into one that resembles the cerebrospinal syphilitic pathology of the tertiary form of the disease. Thus malarial fever therapy acts principally by increasing the defense powers of the brain against syphilitic infection. Without going into details of the effects of heat upon spirochetes in the tissues, it may be stated that high temperature per se is not the sole effective agent in producing beneficial results.

The situation is probably different in the *meningococcic infections*. There is good evidence that the organisms are destroyed by therapeutically elevated temperatures. This also holds true for the *gonococcal infections*, in which artificial fever therapy is definitely curative. In these conditions the mechanism of fever alone is most important in bringing about beneficial results, although other mechanisms may also be brought into play.

The rationale of fever therapy in *multiple sclerosis* is completely obscure. In acute infectious *chorea* (Sydenham's), it is entirely empiric. No contributions to the mechanism of

action of therapeutic fever have been made in the treatment of these conditions by febrile methods. However, it may be fairly stated *that satisfactory results occur in those diseases known to be caused by thermolabile organisms*, and in other conditions little is known about the mechanism.

**Shock.**—In the study of severe reactions and untoward effects of hyperpyrexia, much information has accrued regarding mechanisms of action. The shock syndrome has been described in hyperpyrexia induced by exposure to hot moist air with prevention of loss of heat.<sup>29</sup>

There are *four mechanisms* by means of which *shock*, or *acute failure of the circulation*, may occur during hyperpyrexia. These are as follows: (1) hematogenic, due to the reduction of the volume of blood; (2) vasogenic, due to the effect of heat *per se* on the capillaries; (3) neurogenic, due to stimuli acting through the nervous system; (4) cardiogenic, a probable but not an important factor. Recent investigations stress the importance of a diminished blood volume and an increased permeability, in the production of the shock syndrome. According to Moon's concept, shock may result either from loss of blood or fluid or from atony or dilatation of the vascular walls, especially of the capillaries and venules. Moreover, in hyperpyrexia, increased capillary permeability, with leakage of plasma through the vascular walls, occurs as a result of stasis and anoxemia, still further diminishing the volume of blood.

**Mental Changes.**—Finally, mention should be made of the mental changes which sometimes occur in the course of artificial hyperpyrexia. Ebaugh *et al.*<sup>30</sup> found *delirious episodes* occurring in 10 to 15 per cent of the patients. *Behavior responses*, characterized by elation, anxiety and lethargy, occurred seemingly upon the basis of the individual personality reactions. From clinical observations it was felt that cerebral edema was present during delirious reactions and was particularly evident in the moderate and severe forms. However, the authors emphasized personality, *i. e.*, the habit patterns and other personal characteristics, that comprise the individual

equipment and experience as a major determinant in the clinical pictures obtained under hyperpyrexial treatment.

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